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## Supplementary Table 1. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult multiple exposures.

Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at	Tun	nors <sup>i</sup>	Comments	Reference
	Strain	site	when first dosed	Route, # doses		exposure	death	М	F		
Amitrole	Mice (B6C3F <sub>1</sub> )	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Incidences are mice with	Vesselinovitch, 1983
			Gestation day 12	Diet, to mothers	500 ppm	Gestation day 12 to delivery		6/74 (8%) <sup>c</sup>	0/83 (0%) <sup>c</sup>	adenomas or carcinomas.	
			Newborn	Diet, to mothers	500 ppm	Birth until weaning		10/45 (22%) <sup>c</sup>	0/55 (0%) <sup>c</sup>		
			At weaning	Diet, to offspring	500 ppm	From weaning to 90 weeks		20/55 (36%)°	9/49 (18%) <sup>c</sup>		
Benzidine	Mice (B6C3F <sub>1</sub> )	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/98 (1%)	0/100 (0%)	Higher sensitivity in males during	Vesselinovitch et al., 1975b;
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 to delivery		17/55 (31%) <sup>a</sup>	2/62 (3%) <sup>b</sup>	perinatal period, in females during adulthood.	Vesselinovitch et al., 1979a
			Newborn	Diet, to mothers	150 ppm	Birth until weaning		62/65 (95%) <sup>a</sup>	2/43 (5%) <sup>b</sup>	Incidences are mice with	
			At weaning	Diet, to offspring	150 ppm	From weaning to 90 weeks		22/50 (44%) <sup>a</sup>	47/50 (94%) <sup>a</sup>	adenomas or carcinomas.	
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until weaning		49/49 (100%) <sup>a</sup>	12/48 (25%) <sup>a</sup>		
			Gestation day 12	Diet, to mothers	150 ppm	Gestation day 12 until 90 weeks		50/50 (100%) <sup>a</sup>	47/50 (94%) <sup>a</sup>		
										Continuo	novt nogo

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

<sup>&</sup>lt;sup>1</sup> Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.

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Chemical	Species, Strain	Target site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tum M	ors F	Comments	Reference
DDT Dichlorodiphenyltri chloroethane	Mice (B6C3F1)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/50 (2%)	-		Vesselinovitch et al., 1979b
0.110.100.110			Week 1	Gavage, daily	230 μg	Weeks 1-4		5/49 (10%) <sup>b</sup>	-		
			Week 5	Diet, daily	150 ppm	Weeks 5-90		8/49 (16%) <sup>b</sup>	-		
			Week 1	Gavage, daily until 4 weeks, then in diet	230 µg 150 ppm (diet)	Weeks 1-90		10/50 (20%) <sup>a</sup>	-		
Dieldrin	Mice (B6C3F1)	Liver	Control	None	Control: 0 ppm	N/A	90 weeks	1/58 (2%)	-		Vesselinovitch et al., 1979b
			Week 1	Gavage, daily	12.5 µg	Week 1-4		3/46 (7%) <sup>b</sup>	-		
			Week 5	Diet, daily	10 ppm	Weeks 5-90		7/60 (12%) <sup>b</sup>	-		
			Week 1	Gavage, daily until 4 weeks, then in diet	12.5 µg 10 ppm	Weeks 1-90		21/70 (30%) <sup>a</sup>	-		

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Chemical	Species, Strain	Target site	Age when	Dose Route,	Dose	Duration of exposure	Age at death	Tumo	ors	Comments	Reference
	• · · · · · · · · · · · · · · · · · · ·		first dosed	# doses		onpoou.	uou	M	F		
DEN <sup>ii</sup> Diethylnitrosamine	Rats (Colworth)	Liver	Control		Control	N/A		29/38 (8%		Highest tumor rate when	Peto et al., 1984
			Week 3	Diet (in drinking	16 different doses	From week 3 until death	6 months- 3 years	105/1 (58%		dosed at earlier ages.	
			Week 6	water), daily	combined <sup>iii</sup>	From week 6 until death		714/14 (50%		Incidents are rats with adenomas or carcinomas	
			Week 20			From week 20 until death		76/18 (42%		caromiomas	
		Esophagus	Control		Control	N/A		0/38 ()%			
			Week 3	Diet (in drinking water), daily	16 different doses combined <sup>iv</sup>	From week 3 until death		77/18	30		
			Week 6	water), daily	Combined	From week 6 until death		663/14 (46%			
			Week 20			From week 20 until death		88/18 (49%		Ozni	
										Continuea	, next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Reported as NDEA (N-nitrosodiethylamine) in the original document. Results from each dose are not available.

iv Results from each dose are not available.

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Chemical	Species,	Target	Age	Dose	Dose	<b>Duration of</b>	Age at	Tun	nors	Comments	Reference
	Strain	site	when first dosed	route, # doses		exposure	death	M	F		
DPH Diphenylhyda ntoin, 5,5-	Rats (F344/N)	Liver	dosed Control Perinatal 8 weeks 8 weeks Perinatal Perinatal Control Perinatal 8 weeks Perinatal Control Perinatal Perinatal Perinatal Reveks Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal Perinatal	Control male Diet, male  Control female Diet, female	0 ppm 630 ppm 800 ppm 2400 ppm 630-800 630-2400 ppm 0 ppm 210 ppm 300 ppm 210-100 ppm 210-300 ppm 210 ppm 210 ppm 210 ppm 210 ppm 210-300 ppm 0 ppm 210 ppm 210 ppm	N/A  Perinatal through 8 weeks 8 weeks - 2 years 8 weeks - 2 years Perinatal through 2 years  N/A  Perinatal through 2 years  N/A  Perinatal through 8 weeks 8 weeks - 2 years  Perinatal through 8 weeks - 2 years  Perinatal through 8 weeks 8 weeks - 2 years  Perinatal through 8 weeks - 2 years  Perinatal through 2 years  Perinatal through 2 years  Perinatal through 2 years	2 years 2 years	0/50 (0%) 1/50 (2%) <sup>b</sup> 2/50 (4%) <sup>b</sup> 4/50 (8%) <sup>b</sup> 1/49 (2%) <sup>b</sup> 5/49 (10%) <sup>a</sup> 29/50 (58%) 33/50 (66%) <sup>b</sup> 29/49 (59%) <sup>b</sup> 26/49 (53%) <sup>b</sup> 35/49 (71%) <sup>b</sup> 41/50 (82%) <sup>a</sup>	0/50 (0%) 0/49 (0%) <sup>b</sup> 1/50 (2%) <sup>b</sup> 1/50 (2%) <sup>b</sup> 0/50 (0%) <sup>b</sup> 0/50 (0%) <sup>b</sup> 12/49 (24.5%) <sup>b</sup> 14/49 (28%) <sup>a</sup> 30/50 (60%) <sup>a</sup> 16/50 (32%) <sup>a</sup>	In rats, perinatal exposure ranged from 63-630 ppm, and adult rat exposures ranged from 240-2400 ppm.  In mice, perinatal exposure ranged from 21 to 210 ppm. Adult exposure ranged from 30-300 ppm in males and 60-600 ppm in females.  Tumor incidences are animals with adenomas or carcinomas.	Chhabra et al., 1993b
			Perinatal		210-600 ppm	Perinatal through 2 years			34/50 (68%) <sup>a</sup>	Continued	nevt nage

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at	Tun	nors	Comments	Reference
	Strain	site	when first dosed	route, # doses		exposure	death	М	F		
ETU Ethylene	Rats (F344/N)	Thyroid	Control	Control	0 ppm	N/A	2 years	1/49 (2%)	3/50 (6%)	Tumor incidences are	Chhabra et al., 1992
thiourea	(1 3 1 1/1 1/1		Perinatal	Diet, daily	90 ppm	Perinatal through 8 weeks		4/49 (8%) <sup>b</sup>	3/50 (6%) <sup>b</sup>	animals with adenomas or carcinomas.	.002
			8 weeks		83 ppm	8 weeks – 2 years		12/46 (26%) <sup>a</sup>	7/44 (16%) <sup>b</sup>		
			8 weeks		250 ppm	8 weeks – 2 years		37/50 (74%) <sup>a</sup>	30/49 (61%) <sup>a</sup>		
			Perinatal		90-83 ppm	Perinatal through 2 years		13/50 (26%) <sup>a</sup>	9/47 (19%) <sup>b</sup>		
			Perinatal		90-250 ppm	Perinatal through 2 years		48/50 (96%)	37/50 (74%)		
	Mice (B6C3F <sub>1</sub> )	Liver	Control	Control	0 ppm	N/A	2 years	20/49 (41%)	4/50 (8%)	1111	
	(B0C3F1)		Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		13/49 (26.5%) <sup>b</sup>	5/49 (10%) <sup>b</sup>		
			8 weeks		330 ppm	8 weeks – 2 years		32/50 (64%) <sup>a</sup>	44/50 (88%) <sup>a</sup>		
			8 weeks		1000 ppm	8 weeks – 2 years		46/50 (92%) <sup>a</sup>	48/50 (96%) <sup>a</sup>		
			Perinatal		330-330 ppm	Perinatal through 2 years		34/49 (69%) <sup>a</sup>	46/50 (92%) <sup>a</sup>		
			Perinatal		330-1000 ppm	Perinatal through 2 years		47/49 ((6%) <sup>a</sup>	49/50 (98%) <sup>a</sup>		
		Thyroid	Control	Control	0 ppm	N/A		1/50 (2%)	0/50 (0%)		
			Perinatal	Diet, daily	330 ppm	Perinatal through 8 weeks		1/46 (2%) <sup>b</sup>	1/49 (2%) <sup>b</sup>		
			8 weeks		330 ppm	8 weeks – 2 years		1/49 (2%) <sup>b</sup>	2/50 (4%) <sup>b</sup>		
			8 weeks		1000 ppm	8 weeks – 2 years		29/50 (58%) <sup>a</sup>	38/50 (76%) <sup>a</sup>		
			Perinatal		330-330 ppm	Perinatal through 2 years		2/48 (4%) <sup>b</sup>	10/49 (20%) <sup>a</sup>		
			Perinatal		330-1000 ppm	Perinatal through 2 years		35/49 (71%) <sup>a</sup>	38/50 (76%) <sup>a</sup>		

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Chemical	Species, Strain	Target site	Age when	Dose route,	Dose	Duration of exposure	Age at death	Tum	ors	Comments	Reference
			first dosed	# doses				M	F		
ETU Ethylene	Mice (B6C3F <sub>1</sub> )	Pituitary	Control	Control	0 ppm	N/A	2 years (cont.)	0/44 (0%)	11/47 (23%)	Tumor incidences are	Chhabra et al., 1992
thiourea	,		Perinatal	Diet, daily	330 ppm	Perinatal	, ,	0/42	11/48	animals with	
						through 8		(0%) <sup>b</sup>	(23%) <sup>b</sup>	adenomas or	
						weeks				carcinomas.	
			8 weeks		330 ppm	8 weeks – 2		0/42	19/49		
						years		(0%) <sup>b</sup>	(39%) <sup>b</sup>		
			8 weeks		1000 ppm	8 weeks – 2		8/41	26/49		
						years		(19.5%) <sup>a</sup>	(53%) <sup>a</sup>		
			Perinatal		330-330 ppm	Perinatal		0/45	26/47		
						through 2 years		(0%) <sup>b</sup>	(55%) <sup>a</sup>		
			Perinatal		330-1000	Perinatal		4/39	24/47		
					ppm	through 2 years		(10%) <sup>b</sup>	(51%) <sup>a</sup>		
										Continu	ed, next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species, Strain	Target Site	Age when	Dose Route, # doses	Dose	Duration of	Age at	death	Tumor I	ncidence	Reference
			first dosed			exposure	M	F	М	F	
3- Methylcholanthre	Mice (Albino)	Liver	Control	gavage,3X per week	NA	NA	475 days	480 days	3/39 (7.7%)	0/36 (0%)	Klein, 1959
ne (formerly known as 20-			8 days		0.25 mg/g	10X	311 days	321 days	21/25 (84%) <sup>c</sup>	7/30 (23.3%) <sup>c</sup>	
Methylcholanthrene)		010000100010000000000000000000000000000	90 days		0.25 mg/g	10X	330 days	366 days	1/26 (3.8%) <sup>c</sup>	0/29 (0%) <sup>b</sup>	1
		Lung	Control		NA	NA	475 days	480 days	17/39 (43.6%)	14/36 (38.9%)	
			8 days		0.25 mg/g	10X	311 days	321 days	25/25 (100%) <sup>c</sup>	28/30 (93.3%) <sup>c</sup>	
			90 days		0.25 mg/g	10X	330 days	366 days	25/26 (96.2%) <sup>c</sup>	27/29 (93.1%) <sup>c</sup>	
		Fore- stomach	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10X	311 days	321 days	12/25 (48%) <sup>c</sup>	12/30 (40%) <sup>c</sup>	
			90 days		0.25 mg/g	10X	330 days	366 days	13/26 (50%) <sup>c</sup>	8/29 (27.6%) <sup>c</sup>	
		Skin	Control		NA	NA	475 days	480 days	0/39 (0%)	0/36 (0%)	
			8 days		0.25 mg/g	10X	311 days	321 days	4/25 (16%) <sup>c</sup>	4/30 (13.3%) <sup>c</sup>	
			90 days		0.25 mg/g	10X	330 days	366 days	1/26 (3.8%) <sup>c</sup>	1/25 (4%) <sup>c</sup>	

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at	Tur	nors	Comments	Reference
	Strain	site	when first	route, # doses		exposure	death	M	F		
			dosed								
PBBs Polybrominated	Rats (F344/N)	Liver <sup>v</sup>	Control	Control	0 ppm	N/A	2 years	1/50 (2%)	0/50 (0%)	Findings suggest that combined	Chhabra et al., 1993a
biphenyls	(F344/IN)		Perinatal	Diet	10 ppm	Perinatal – 8 weeks		(2%) 5/50 (10%) <sup>b</sup>	0/50 (0%) <sup>b</sup>	perinatal and adult exposure	1993a
			8 weeks		10 ppm	8 weeks – 2 years		`12/49 (24%) <sup>a</sup>	12/50 (24%) <sup>a</sup>	increases PBB- related	
			8 weeks		30 ppm	8 weeks – 2		41/50	39/50	hepatocellular	
			Perinatal		10-10 ppm	years Perinatal – 2		(82%) <sup>a</sup> 16/50	(78%) <sup>a</sup> 39/50	carcinogenicity relative to adult-	
			Perinatal		10-30 ppm	years Perinatal – 2		(32%) <sup>a</sup> 41/50	(78%) <sup>a</sup> 47/50	only exposure in mice and female	
						years		(82%) <sup>a</sup>	(94%) <sup>a</sup>	rats.	
		Mononucle	Control	Control	0 ppm	N/A	2 years	25/50	14/50		
		ar cell						(50%)	(28%)	Apparent	
		leukemia (MCL)	Perinatal	Diet	10 ppm	Perinatal – 8 weeks		31/50 (62%) <sup>b</sup>	13/50 (26%) <sup>b</sup>	association between	
		, ,	8 weeks		10 ppm	8 weeks – 2 years		33/50 (66%) <sup>a</sup>	22/50 (44%) <sup>b</sup>	increasing incidences of MCL	
			8 weeks		30 ppm	8 weeks – 2		31/50	23/50	and exposure to PBB in male and	
			Perinatal		10-10 ppm	years Perinatal – 2		(62%) <sup>b</sup> 37/50	(46%) <sup>a</sup> 27/50	female rats.	
			Perinatal		10-30 ppm	years Perinatal – 2		(74%) <sup>a</sup> 37/50	(54%) <sup>a</sup> 25/50	Tumor incidences	
				_	10-30 ppiii	years		(74%) <sup>a</sup>	(50%) <sup>a</sup>	are animals with	
	Mice (B6C3F <sub>1</sub> )	Liver <sup>vi</sup>	Control	Control	0 ppm	N/A	2 years	16/50 (32%)	5/50 (10%)	adenomas or carcinomas	
	(B0C3F1)		Perinatal	Diet	30 ppm	Perinatal – 8		40/50	21/50	caromornas	
						weeks		(80%) <sup>a</sup>	(42%) <sup>a</sup>		
			8 weeks		10 ppm	8 weeks – 2 years		48/49 (98%) <sup>a</sup>	42/50 (84%) <sup>a</sup>		
			8 weeks		30 ppm	8 weeks – 2 years		48/50 (96%) <sup>a</sup>	47/48 (98%) <sup>a</sup>		
			Perinatal		10 ppm	Perinatal – 2		46/49	44/50		
			Perinatal		30-30 ppm	years Perinatal – 2		(94%) <sup>a</sup> 50/50	(88%) <sup>a</sup> 47/47		
					• •	years		(100%) <sup>a</sup>	(100%) <sup>a</sup>		
									·	Continued	, next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

<sup>&</sup>lt;sup>v</sup> Tumors were adenomas or carcinomas. <sup>vi</sup> Tumors were adenomas or carcinomas.

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Chemical	Species,	Target	Age	Dose route,	Dose	Duration of	Age at	Tu	mors	Comments	Reference
	Strain	site	when first	# doses		exposure	death	M	F		
Safrole	Mice (B6C3F <sub>1</sub> )	Liver	<b>dosed</b> Control	None	None	N/A	90 weeks	3/100 (3%)	0/100 (0%)	Highest tumor rate in males due	Vesselinovitch et al., 1979b
			Day 12 of gestation	Gavage, to mothers	120 µg/g body weight	4x (days 12, 14, 16, 18)		2/61 (3%) <sup>b</sup>	0/65 (0%) <sup>b</sup>	to preweaning treatment.  Highest tumor	
			Newborn	Gavage, to mothers, on alternate days	120 µg/g body weight	From birth until weaning		28/83 (34%) <sup>a</sup>	2/80 (3%) <sup>b</sup>	rate in females due to susceptibility in adulthood.	
			At weaning	Gavage, to offspring, 2x weekly	120 μg/g body weight	From weaning until 90 weeks		4/35 (11%) <sup>b</sup>	22/36 (61%) <sup>a</sup>	Tumor incidences ae mice with	
			Day 12 of gestation	Gavage, to mothers, alternate days	120 µg/g body weight	From gestation until weaning		22/68 (32%) <sup>c</sup>	1/72 (1%) <sup>c</sup>	adenomas or carcinomas.	
			Day 12 of gestation	Gavage, to mothers, alternate days until weaning; Gavage, to offspring, 2x weekly	120 µg/g body weight	From gestation until 90 weeks		19/37 (51%) <sup>c</sup>	37/46 (80%) <sup>c</sup>		
Urethane	Mice (B6AF1/J)	Liver	1 week	gavage	2.5 mg/pup 2.5 mg/pup	1x  16x (1x at 1 week; 3x weekly for 5 weeks beginning at 4 wks of age)	39-40 weeks 39 weeks	12/37 (33%)° 11/33 (33%)°	0/40 (0%) <sup>c</sup> 0/31 (0%) <sup>c</sup>	No tumor data for controls	Klein, 1966
			4 weeks		2.5 mg/pup	15x (3x weekly for 5 weeks beginning at 4 weeks of age)	41 weeks	0/37 (0%) <sup>c</sup>	0/31 (0%) <sup>c</sup>		
						<i>3</i> /				Continued	, next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target	Age when	Dose	Dose	Duration	Age at	Tum	ors	Comments	Reference			
	Strain	site	first dosed	route, # doses		of exposure	death	М	F					
C nyl Chloride	Rats (Sprague-	Liver angio-	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)	Higher tumor risk when	Maltoni et al. 1984			
	Dawley)	sarcoma	Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	5/18 (28%) <sup>c</sup>	12/24 (50%) <sup>c</sup>	exposed at birth, higher for				
					10,000 ppm	5 weeks		6/24 (25%) <sup>c</sup>	9/20 (45%)°	females.				
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	3/17 (18%)°	10/25 (40%)°	<b></b>				
					10,000 ppm	52 weeks		3/21 (14%) <sup>c</sup>	4/25 (16%) <sup>c</sup>					
		Zymbal gland	Control	Control	0 ppm	N/A	135 weeks	0/28 (0%)	0/29 (0%)					
		-	Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/12 (8%) <sup>c</sup>	1/17 (6%) <sup>c</sup>					
					10,000 ppm	5 weeks		1/17 (6%) <sup>c</sup>	0/17 (0%) <sup>c</sup>	nn				
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	3/29 (10%) <sup>c</sup>	4/30 (13%) <sup>c</sup>					
					10,000 ppm	52 weeks		10/30 (33%)°	6/30 (20%) <sup>c</sup>	•••				
		Leukemia	Control	Control	0 ppm	N/A	135 weeks	0/27 (0%)	1/29 (3%)					
		Leukemia	Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	N/A	1/7 (14%) <sup>c</sup>					
					10,000 ppm	5 weeks		2/6 (33%) <sup>c</sup>	0/15 (0%) <sup>c</sup>	•••				
		-	Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	N/A	0/29 (0%) <sup>c</sup>					
			***************************************	N	NI L				10,000 ppm	52 weeks		0/27 (0%) <sup>c</sup>	2/29 (7%) <sup>c</sup>	•••
	Nephro- blastoma	Nephro- blastoma	Control	Control	0 ppm	N/A	135 weeks	0/22 (0%)	0/29 (0%)					
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	0/15 (0%) <sup>c</sup>	0/21 (0%) <sup>c</sup>					
				10,000 ppm	5 weeks		0/19 (0%) <sup>c</sup>	0/17 (0%) <sup>c</sup>	•••					
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	4/18 (22%) <sup>c</sup>	1/26 (4%) <sup>c</sup>					
					10,000 ppm	52 weeks		3/21 (14%) <sup>c</sup>	2/25 (8%) <sup>c</sup>					
		Angio- sarcomas: other sites	Control	Control	0 ppm	N/A	135 weeks	0/29 (0%)	0/29 (0%)					

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tun M	nors F	Comments	Reference
/C /inyl Chloride	Rats (Sprague-	Angio- sarcomas:	Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/15 (7%) <sup>c</sup>	0/21 (0%) <sup>c</sup>		Maltoni et al., 1984
	Dawley	other sites			10,000 ppm	5 weeks		0/19 (0%)	0/17 (0%) <sup>c</sup>		
			Week 13		6,000 ppm	4 hrs/day,	135 weeks	1/29	2/30		
					10.000	5 days/wk,		(3%) <sup>c</sup>	(7%) <sup>c</sup>		
					10,000 ppm	52 weeks		2/30 (7%) <sup>c</sup>	1/30 (3%) <sup>c</sup>		
		Angiomas	Control	Control	0 ppm	N/A	135 weeks	0/28	2/29		
		and	Control	Control	о рр	14/71	roo moono	(0%)	(7%) <sup>c</sup>		
		fibromas:	Newborn	Inhalation	6,000 ppm	4 hrs/day,	124 weeks	1/15	0/21		
		other sites			10.000	5 days/wk,		(7%) <sup>c</sup>	(0%) <sup>c</sup>		
					10,000 ppm	5 weeks		2/19 (11%) <sup>c</sup>	1/17 (6%) <sup>c</sup>		
			Week 13		6,000 ppm	4 hrs/day,	135 weeks	2/29	2/30		
			WOOK 10		0,000 ррпп	5 days/wk,	100 WOOKS	(7%) <sup>c</sup>	(7%) <sup>c</sup>		
					10,000 ppm	52 weeks		2/29	1/29		
								(7%) <sup>c</sup>	(3%) <sup>c</sup>		
		Hepatoma	Control	Control	0 ppm	N/A	135 weeks	0/19 (0%)	0/28 (0%)		
		•	Newborn	Inhalation	6,000 ppm	4 hrs/day,	124 weeks	9/18	11/24		
				a.a	о,ооо рр	5 days/wk,	noone	(50%) <sup>c</sup>	(46%) <sup>c</sup>		
					10,000 ppm	5 weeks		13/24	7/20		
								(54%) <sup>c</sup>	(35%) <sup>c</sup>	118	
			Week 13		6,000 ppm	4 hrs/day, 5 days/wk,	135 weeks	0/10 (0%) <sup>c</sup>	1/17 (6%) <sup>c</sup>		
					10,000 ppm	52 weeks		1/8	0/16		
								(13%) <sup>c</sup>	(0%) <sup>c</sup>		
		Skin	Control	Control	0 ppm	N/A	135 weeks	0/20	1/29		
		carinomas	NI a codo a ma	labalatian	0.000	4 1 /-1	404	(0%)	(3%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day, 5 days/wk,	124 weeks	1/10 (10%) <sup>c</sup>	1/14 (7%) <sup>c</sup>		
					10,000 ppm	5 weeks		1/16	0/15		
					- /   -   -   - / ·			(6%) <sup>c</sup>	(0%) <sup>c</sup>		
			Week 13		6,000 ppm	4 hrs/day,	135 weeks	0/15	2/19	<del></del>	
					40.000	5 days/wk,		(0%) <sup>c</sup>	(11%) <sup>c</sup>		
	Neuro-				10,000 ppm	52 weeks		2/13 (15%) <sup>c</sup>	1/21 (5%) <sup>c</sup>		
		Neuro-	Control	Control	0 ppm	N/A	135 weeks	0/22	0/29		
		blastoma	20		- hh		. 50	(0%)	(0%)		
			Newborn	Inhalation	6,000 ppm	4 hrs/day,	124 weeks	0/18	0/29		
						5 days/wk,		(0%) <sup>c</sup>	(0%) <sup>c</sup>		
					10,000 ppm	5 weeks		0/22	0/19		

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Chemical	Species,	Target	Age when	Dose	Dose	Duration	Age at	Tum	ors	Comments	Reference
	Strain	site	first dosed	route, # doses		of exposure	death	M	F		
VC Vinyl Chloride	Rats (Sprague- Dawley	Neuro- Blastoma	Week 13		6,000 ppm 10,000 ppm	4 hrs/day, 5 days/wk, 52 weeks	135 weeks	2/21 (10%) <sup>c</sup> 2/22 (9%) <sup>c</sup>	1/27 (4%) <sup>c</sup> 5/26 (19%) <sup>c</sup>		Maltoni et al., 1984

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Supplementary Table 2. Methodological information and tumor incidence for animal studies with early postnatal and juvenile and adult acute exposure.

Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at	Tum	ors <sup>vii</sup>	Comments	Reference
	Strain	site	when first dosed	route, # doses		exposure	death	M	F		
Benzo(a)pyrene	Mice (B6C3F <sub>1</sub> )	Liver	Control	Control	None	N/A	142 weeks	7/100 (7%)	1/100 (1%)	In general, hepatomas	Vesselinovitch et al., 1975a
	, , ,		Day 1	IP <sup>viii</sup>	75 μg/g body weight	1x	86 weeks (m) 129 weeks (f)	26/47 (55%) <sup>c</sup>	3/45 (7%)°	developed with significantly higher incidence (p<0.01) in mice	,
					150 μg/g body weight	1x	81 weeks (m) 121 weeks (f)	51/63 (81%) <sup>c</sup>	8/45 (18%) <sup>c</sup>	that were treated within 24 hours of birth or at 15 days of	
			Day 15	IP	75 μg/g body weight	1x	93 weeks (m) 116 weeks (f)	36/60 (60%) <sup>c</sup>	4/55 (7%) <sup>c</sup>	age than they did in similarly treated animals at 42 days of	
		Do	Day 42		150 µg/g body weight	1x	81 weeks (m) 90 weeks (f)	32/55 (58%) <sup>c</sup>	4/55 (7%) <sup>c</sup>	age. + higher for	
			Day 42	IP	75 μg/g body weight	1x	108 weeks(m)	7/55 (13%) <sup>c</sup>	0/47 (0%) <sup>c</sup>	males	
					150 µg/g body weight	1x	87 weeks (m)	4/47 (9%) <sup>c</sup>	0/46 (0%) <sup>c</sup>		
Benzo(a)pyrene	Mice (C3A F <sub>1</sub> )	Liver	Control	Control	None	N/A	142 weeks	8/100 (8%)	1/100 (1%)	+ higher for males	
			Day 1	IP	75 μg/g body weight	1x	80 weeks (m) 91 weeks (f)	21/62 (34%) <sup>c</sup>	1/45 (2%) <sup>c</sup>	"Age at death" is the average	
	150 μg/g 1x 69 weeks 24/52 1/56 age a body weight (m) (46%) <sup>c</sup> (2%) <sup>c</sup> tumor	age at which tumors were observed.									
			Day 15	IP	75 μg/g body weight	1x	90 weeks (m) 102 weeks (f)	15/56 (27%) <sup>c</sup>	1/49 (2%) <sup>c</sup>		

vii Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified. viii Intraperitoneal injection (IP)

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at	Tum	ors <sup>ix</sup>	Comments	Reference
	Strain	site	when first dosed	route, # doses		exposure	death	M	F		
Benzo(a)pyrene	Mice (C3A F <sub>1</sub> )	Liver		IP	150 µg/g body weight	1x	77 weeks (m) 62 weeks (f)	12/53 (23%) <sup>c</sup>	1/57 (2%) <sup>c</sup>		
			Day 42	IP	75 μg/g body weight	1x	,,	0/30 (0%) <sup>c</sup>	0/32 (0%) <sup>c</sup>		
					150 µg/g body weight	1x	79 weeks (m)	1/32 (3%) <sup>b</sup>	0/40 (0%) <sup>c</sup>		
Benzo(a)pyrene	Mice (B6C3F <sub>1</sub> )	Lung	Control	Control	Control	N/A	142 weeks	13/100 (13%)	9/100 (9%)	Both sexes developed lung	
			Day 1	IP	75 μg/g body weight	1x	103 weeks(m) 126 weeks (f)	20/47 (43%) <sup>c</sup>	22/45 (49%) <sup>c</sup>	tumors with higher incidence when treated with B(a)P at birth than at 15	
					150 µg/g body weight	1x	84 weeks(m) 112 weeks (f)	37/63 (59%) <sup>c</sup>	28/45 (62%) <sup>c</sup>	or 42 days of age (p<0.05).	
			Day 15	ΙP	75 μg/g body weight	1x	103 weeks(m) 122 weeks (f)	15/60 (25%) <sup>c</sup>	18/55 (33%) <sup>c</sup>		
					150 µg/g body weight	1x	82 weeks(m) 101 weeks (f)	20/55 (36%) <sup>c</sup>	18/45 (40%) <sup>c</sup>		
			Day 42	IP	75 μg/g body weight	1x	119 weeks(m) 131 weeks (f)	20/55 (36%)°	12/47 (26%) <sup>c</sup>		
					150 µg/g body weight	1x	95 weeks(m) 118 weeks (f)	18/47 (38%) <sup>c</sup>	8/46 (17%) <sup>c</sup>		
										Continued, n	ext page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

ix Where not delineated by gender, data combined by study authors or gender not specified. Where percentages only are given, number of subjects not specified.

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age at death	Tun	nors	Comments	Reference
	Strain	site	when first	route, # doses		exposure		M	F		
			dosed								
Benzo(a)pyrene	Mice (C3A F <sub>1</sub> )	Lung	Control	Control	None	N/A	142 weeks	60/100 (60%)	50/100 (50%)	Of the 2 mouse strains tested,	Vesselinovitch et al., 1975a
			Day 1	IP	75 µg/g body weight	1x	78 weeks(m) 82 weeks (f)	58/62 (93%) <sup>c</sup>	42/45 (93%) <sup>c</sup>	C3AF1 mice developed	
					150 µg/g body weight	1x	70 weeks(m) 73 weeks (f)	48/52 (92%)°	52/56 (93%) <sup>c</sup>	significantly more tumors than did	
			Day 15	IP	75 µg/g body weight	1x	87 weeks(m) 98 weeks (f)	52/56 (93%)°	46/49 (94%) <sup>c</sup>	the B6C3F1 mice (p<0.001)	
					150 µg/g body weight	1x	75 weeks(m) 79 weeks (f)	50/53 (94%)°	52/57 (91%) <sup>c</sup>	(p 101001)	
			Day 42	IP	75 µg/g body weight	1x	91 weeks(m) 93 weeks (f)	28/30 (93%)°	28/32 (87%) <sup>c</sup>		
					150 µg/g body weight	1x	85 weeks(m) 83 weeks (f)	28/32 (87%) <sup>c</sup>	36/40 (90%)°		
DBA	Mice	Lung	Control	Control	None	N/A	228 days	1/31 (			Law, 1940
Dibenzanthracene	(Caracul x P stock)	Lung	Day 1	IP	4 mg per cm <sup>3</sup> vehicle	1x	181 days		100%)°		Law, 1940
	. στοστή		2 months	SC <sup>x</sup>	4 mg per cm <sup>3</sup> vehicle	1x	189 days	2/29 (	6.9%) <sup>c</sup>		
DEN	Mice	Liver	Control	Control	Vehicle	4x	142 weeks(m)	7/98	1/100	Animals treated	Vesselinovitch
Diethylnitrosamine	(B6C3F <sub>1</sub> )				(0.01 ml trioctanoin/g		137 weeks (f)	(7%)	(1%)	as newborns and infants	et al., 1984
					body weight)					developed	
			Day 1	IP (3-, 6-	1.5 μg/g	4x	67 weeks (m)	37/51	45/64	significantly more	
				and 6-day	body weight		90 weeks (f)	(73%) <sup>c</sup>	(70%) <sup>c</sup>	liver tumors than	
				intervals)	3 μg/g body	4x	65 weeks (m)	40/58	44/65	animals that	
			Day 15		weight 1.5 µg/g	4ν	80 weeks (f) 86 weeks (m)	(69%) <sup>c</sup> 41/57	(68%) <sup>c</sup> 40/71	were treated as young adults.	
			Day 15		body weight	4x	117 weeks (f)	(72%)°	(56%) <sup>c</sup>	young addits.	
					3 µg/g body	4x	76 weeks (m)	48/69	46/62	Newborns and	
					weight	iA.	96 weeks (f)	(70%)°	(74%) <sup>c</sup>	infant females	
			Day 42		1.5 µg/g	4x	117 weeks(m)	9/49	1/47	developed liver	
			,		body weight		135 weeks (f)	(18%) <sup>c</sup>	(2%) <sup>c</sup>	tumors at a later	
					3 μg/g body weight	4x	123 weeks(m) 133 weeks (f)	6/38 (16%) <sup>c</sup>	4/57 (7%) <sup>c</sup>	age than similarly treated males.	
					ū		,	, ,		Incidences for malignant tumors only.  Continued, r.	neyt nage

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

<sup>&</sup>lt;sup>x</sup> Subcutaneous injection (SC)

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Chemical	Species,	Target	Age	Dose	Dose	Duration	Age at	Tun	nors	Comments	Reference
	Strain	site	when first dosed	route, # doses		of exposure	death	M	F		
DEN Diethylnitrosamin e	Mice (C3AF <sub>1</sub> )	Liver	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4x	123 weeks(m) 131weeks (f)	8/99 (8%)	1/97 (1%)	Highest tumor rate when dosed at early ages.	Vesselinovitch et al., 1984
			Day 1	IP (3-, 6- and 6-	1.5 µg/g body weight	4x	64 weeks (m) 84 weeks (f)	23/32 (72%) <sup>c</sup>	11/39 (28%) <sup>c</sup>	Newborns and infant females	
				day intervals)	3 μg/g body weight	4x	59 weeks (m) 76 weeks (f)	39/58 (67%) <sup>c</sup>	26/50 (52%) <sup>c</sup>	developed liver tumors at a lower	
			Day 15	,	1.5 µg/g body weight	4x	82 weeks (m) 102 weeks (f)	22/46 (48%) <sup>c</sup>	`8/65 (12%) <sup>c</sup>	incidence than similarly treated	
					3 μg/g body weight	4x	74 weeks (m) 94 weeks (f)	35/54 (65%) <sup>c</sup>	22/62 (35%) <sup>c</sup>	males.	
			Day 42		1.5 µg/g body weight	4x	105 weeks(m) 106 weeks (f)	12/56 (22%)°	0/53 (0%)°	+ higher for males	
					3 μg/g body weight	4x	105 weeks(m) 103 weeks (f)	9/57 (16%)°	0/56 (0%) <sup>c</sup>		
	Mice (B6C3F <sub>1</sub> )	Lung	Control	Control	Vehicle (0.1 trioctanoin/g body weight)	4x	142 weeks(m) 137 weeks (f)	13/98 (13%)	9/100 (9%)	The mice treated as newborns showed lung tumors earlier than animals	
			Day 1	IP (3-, 6- and 6-	1.5 μg/g body weight	4x	70 weeks (m) 91 weeks (f)	29/51 (57%) <sup>c</sup>	49/64 (77%) <sup>c</sup>	exposed at other times. It is not	
				day intervals)	3 μg/g body weight	4x	68 weeks (m) 81 weeks (f)	34/58 (59%)°	42/65 (65%)°	known whether this was due to actual earlier emergence of tumors or to their earlier detection caused by shorter survival.	

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Chemical	Species,	Target	Age	Dose	Dose	Duration	Age at death	Tum	ors	Comments	Reference
	Strain	site	when first dosed	route, # doses		of exposure		M	F		
	Mice (B6C3F <sub>1</sub> )	Lung (cont.)	Day 15	IP (3-,6- and 6-	1.5 µg/g body weight	4x	87 weeks (m) 115 weeks (f)	51/57 (89%)°	61/71 (86%) <sup>c</sup>		
	(cont.)			day intervals)	3 µg/g body	4x	77 weeks (m) 97 weeks (f)	51/69 (74%) <sup>c</sup>	53/62 (85%) <sup>c</sup>		
			Day 42	iiileivais)	weight 1.5 µg/g	4x	123 weeks(m)	38/49	38/47		
			- wy		body weight		129 weeks (f)	(78%) <sup>c</sup>	(81%) <sup>c</sup>		
					3 µg/g body	4x	121 weeks(m)	33/38	43/57		
					weight		127 weeks (f)	(87%) <sup>c</sup>	(75%) <sup>c</sup>		
	Mice	Lung	Control	Control	Vehicle (0.1	4x	142 weeks(m)	60/99	50/97	Of the two	
	(C3AF <sub>1</sub> )				trioctanoin/g body weight)		137weeks (f)	(61%)	(52%)	strains, C3AF1 mice	
			Day 1	IP (3-, 6- and 6-	1.5 µg/g body weight	4x	65 weeks (m) 84 weeks (f)	30/32 (94%) <sup>c</sup>	38/39 (97%) <sup>c</sup>	developed lung tumors with a	
				day	3 µg/g body	4x	59 weeks (m)	49/58	46/50	higher	
				intervals)	weight		76 weeks (f)	(84%) <sup>c</sup>	(92%) <sup>c</sup>	incidence and	
			Day 15	,	1.5 µg/g	4x	80 weeks (m)	42/46	`61/6Ś	multiplicity	
			-		body weight		101 weeks (f)	(91%) <sup>c</sup>	(94%) <sup>c</sup>	than B6C3F1	
					3 µg/g body	4x	74 weeks (m)	50/54	57/62	hybrids.	
					weight		92 weeks (f)	(93%) <sup>c</sup>	(92%) <sup>c</sup>		
			Day 42		1.5 μg/g	4x	104 weeks(m)	55/56	52/53		
					body weight		110 weeks (f)	(98%) <sup>c</sup>	(98%) <sup>c</sup>		
					3 µg/g body	4x	101 weeks(m)	56/57	54/56		
					weight		102 weeks (f)	(98%) <sup>c</sup>	(96%) <sup>c</sup>		
										Continued, n	ext page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species	Target	Age	Dose	Dose	Duration of	Age at	Tun	nors	Comments	Reference
	, Strain	site	when first dosed	route, # doses		exposure	death	М	F		
DEN Diethylnitrosamine	Mice (B6C3F <sub>1</sub> )	Liver	Control	Control	None	N/A	90 weeks	1/98 (1%)	0/96 (0%)	Infant animals of both sexes (Day	Vesselinovitch and
			Gestatio n day 18	IP	1.5 µg/g body weight	1x		2/50 (4%) <sup>c</sup>	1/51 (2%) <sup>c</sup>	15) were more sensitive than	Mihailovich, 1983
			Day 15	IP (3-, 6- and 6-day	1.5 µg/g body weight	4x		47/51 (92%) <sup>c</sup>	60/64 (94%) <sup>c</sup>	similarly exposed adults.	
			Day 42	intervals)	1.5 µg/g body weight	4x		13/49 (26%)°	3/47 (6%) <sup>c</sup>		
	***************************************		Day 1	IP	1.5 μg/g body weight	1x	73 weeks	15/59 (25%) <sup>c</sup>	-	At the 1.5 µg dose level, 1-day-old	Vesselinovitch et al., 1979a
					5 μg/g body weight	1x		29/45 (64%) <sup>c</sup>	-	mice developed significantly fewer	orall, 1070a
					10 µg/g body weight	1x		24/25 (96%) <sup>c</sup>	-	liver tumors than similarly treated	
			Day 15	IP	1.5 µg/g body weight	1x		13/24 (54%) <sup>c</sup>	-	infants (Day 15) (p<0.025).	
					5 μg/g body weight	1x		40/54 (74%) <sup>c</sup>	-	Tumor incidence	
					10 μg/g body weight	1x		25/25 (100%)°	-	in treated groups versus controls was not evaluated.	
											_
DMBA Dimethyl-	Rats (Sprague-	Mammary adeno-	Day 20	Gavage	10 mg/100 g body weight	1x	Week 25	-	3/6 (50%) <sup>c</sup>	36 of 42 (86%) animals dosed at	Russo et al., 1979
benz(a)anthracene	Dawley)	sarcoma	Day 30		10 mg/100 g body weight	1x	Week 26	-	14/15 (93%) <sup>c</sup>	age 20 days died soon after.	
			Day 40		10 mg/100 g body weight	1x	Week 27	-	8/9 <sup>°</sup> (89%) <sup>°</sup>	Highest number of	
			Day 46		10 mg/100 g body weight	1x	Week 28	-	8/8 <sup>°</sup> (100%) <sup>c</sup>	tumors per animal was in the 46-day	
			Day 55		10 mg/100 g body weight	1x	Week 29	-	33/34 (97%)°	group, with decreasing	
			Day 70		10 mg/100 g body weight	1x	Week 32	-	5/8 (63%)°	numbers in the older animals.	
			Day 140		10 mg/100 g body weight	1x	Week 42	-	10/15 (67%) <sup>c</sup>	Animals were	
			Day 180		10 mg/100 g body weight	1x	Week 47	-	14/26 (54%) <sup>c</sup>	sacrificed 22 weeks after treatment.	
										Continued, i	next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target site	Age when	Dose	Dose	Duration	Age at	Tun	nors	Comments	Reference
	Strain		first dosed	route, # doses		of exposure	death	M	F		
DMBA	Rats	Mammary carcinoma <sup>xi</sup>	Control 5-8 weeks	Control	None	N/A	17 months	0/22	0/25 (0%)	Highest tumor rate in females	Meranze et al., 1969
Dimethyl- benz(a)anthracene	(Wistar)	carcinoma	Control	Control	None	N/A	20 months	(0%) 0/31	2/20	exposed at 5-8	ai., 1969
Deliz(a)alillilacelle			26 weeks	Control	None	IN/A	20 1110111115	(0%)	(10%)	weeks.	
			< Week 2	Gavage	0.5-1.0 mg	1x	Week 40-56	0/23	4/50	WCCNG.	
			\ \\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\\	Ouvago	0.0 1.0 1119	17	7700K 10 00	(0%) <sup>c</sup>	(8%) <sup>c</sup>	Animals were	
			Week 5-8		15 mg	1x	Week 14-55	0/23	14/25	observed for 16	
								(0%) <sup>c</sup>	(56%)°	months	
			Week 26		15 mg	1x	Week 32-73	0/34	4/26	following	
					· ·			(0%) <sup>c</sup>	(15%) <sup>c</sup>	treatment.	
	Rats	Mammary	Week 5-8	Gavage	15 mg	1x	Week 14-55	0/21	0/22		
	(Wistar,	carcinoma		J	Ü			(0%) <sup>c</sup>	(0%) <sup>c</sup>		
	castrated)		Week 26		15 mg	1x	Week 32-73	0/33	0/26		
					_			(0%) <sup>c</sup>	(0%) <sup>c</sup>		
	Rats	Total tumors	Control	Control	None	N/A	17 months	0/22	0/25	Total tumors	
	(Wistar)		5-8 weeks					(0%)	(0%)	includes	
			Control	Control	None	N/A	20 months	2/31	5/20	leukemia.	
			26 weeks	_				(6%)	(25%)		
			< Week 2	Gavage	0.5-1.0 mg	1x	Week 40-56	16/23	36/50		
			\\\ \   = 0		4=			(70%) <sup>c</sup>	(72%) <sup>c</sup>		
			Week 5-8		15 mg	1x	Week 14-55	7/23	16/25		
			M1-00		45	4	W1- 00 70	(30%) <sup>c</sup>	(64%) <sup>c</sup>		
			Week 26		15 mg	1x	Week 32-73	12/34	13/26 (50%)°		
	Mice	Luca	Control	Control	Λαιιοοιιο	4.2	40 woolso	(35%) <sup>c</sup>		15 ua DMDA	Wolton 1066
	(BALB/c)	Lung	Control:	Control SC	Aqueous gelatine	1x	40 weeks	0/12 (0%)	7/23 (30%)	15 µg DMBA	Walters, 1966
	(DALD/C)		Day 1 Day 1	SC	gelatine 15 μg	1x	40 weeks <sup>xii</sup>	14/14	24/24	gave rise to a significantly	
			Day I	30	15 µg	1.8	40 WEEKS	(100%) <sup>c</sup>	(100%) <sup>c</sup>	greater	
			Week 2-3	SC	15 µg	1x	42-43 weeks	12/23	16/22	incidence of	
			(suckling)	00	то ру	17	12 10 WOOKO	(52%)°	(73%) <sup>c</sup>	lung tumors	
			(Guoitii 19)	SC	30 µg	2x	42-43 weeks	14/14	24/24	when	
					(60 µg total)			(100%) <sup>c</sup>	(100%) <sup>c</sup>	administered to	
			Adult <sup>xiii</sup>	SC	15 μg	1x	48-49 weeks	6/12	15/33	newborn mice	
					1.5			(50%) <sup>c</sup>	(45%) <sup>c</sup>	than to suckling	
				SC	30 µg	2x	48-49 weeks	9/10	21/23	or young adults.	
					(60 µg total)			(90%) <sup>c</sup>	(91%) <sup>c</sup>	, ,	
				SC	30 µg	6x	48-49 weeks	12/12	13/13		
					(180 µg total)			(100%) <sup>c</sup>	(100%) <sup>c</sup>		
										Continued n	

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

xii Study also included mammary fibroadenomas and fibromas, as well as other types of cancers. xiii Includes survivors up to 40 weeks only. xiii 8-9 weeks old.

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Chemical	Species, Strain	Target site	Age when first dosed	Dose route, # doses	Dose	Duration of exposure	Age at death	Tumors M F	Comments	Reference
DMBA Dimethyl-	Mice (Swiss)	Lymphoma	Control	Control	None	N/A	31-52 weeks	3/408 (0.7%)	Higher tumor rates at younger age of	Pietra et al., 1961
benz(a)anthracen e	,		Day 1	IP	30-40 μg	1x	13-33 weeks	`6/31 <sup>´</sup> (19%) <sup>c</sup>	exposure.	
			Day 1	SC	30-40 μg	1x	12-27 weeks	8/27 (30%)°	Only one treatment group was exposed IP;	
			Week 8	SC	900 µg	1x	30 weeks	1/13 (8%)°	others were exposed by subcutaneous injection.	
	Mice (Swiss)	Lung	Control	Control	None	N/A	31-52 weeks	4/408 (0.9%)	•	
	,		Day 1	IP	30-40 μg	1x	13-33 weeks	24/31 <sup>°</sup> (77%)°		
			Day 1	SC	30-40 μg	1x	12-27 weeks	23/27 (85%)°		
			Week 8	SC	900 µg	1x	30 weeks	2/13 (15%) <sup>c</sup>		
DMN	Rats	Kidney	Day 1	ΙP	20 mg/kg	1x	> 5 months	1/33 (3) <sup>c</sup>	In the neonatal group,	Hard, 1979
Dimethyl-	(Wistar)	carcinoma	Day 21		30 mg/kg	1x		5/39 (13) <sup>c</sup>	the dose was reduced	
nitrosamine			Month 1		30 mg/kg	1x		2/33 (6) <sup>c</sup>	to 20 mg/kg in order to	
			Month 1.5		30 mg/kg	1x		1/28 (4) <sup>c</sup>	achieve approximately	
			Month 2		30 mg/kg	1x		1/26 (4) <sup>c</sup>	equivalent numbers of	
			Month 3		30 mg/kg	1x		10/27 (37) <sup>c</sup>	survivors.	
			Month 4		30 mg/kg	1x		7/32 (22) <sup>c</sup>	No control group.	
		•••	Month 5		30 mg/kg	1x		0/14 (0) <sup>c</sup>	No control group.	ne.
	Rats	Kidney	Day 1	ΙP	20 mg/kg	1x	≥ 5 months	1/33 (3) <sup>c</sup>		
	(Wistar)	adenoma	Day 21		30 mg/kg	1x		13/39 (33) <sup>c</sup>		
			Month 1		30 mg/kg	1x		11/33 (33) <sup>c</sup>		
			Month 1.5		30 mg/kg	1x		13/28 (48) <sup>c</sup>		
			Month 2		30 mg/kg	1x		11/26 (42) <sup>c</sup>		
			Month 3		30 mg/kg	1x		18/27 (67) <sup>c</sup>		
			Month 4		30 mg/kg	1x		17/32 (53)°		
	Data	I/: al.a a	Month 5	IP	30 mg/kg	1x		6/14 (43) <sup>c</sup>	Managabumaltuman	10
	Rats (Wistar)	Kidney mesenchym	Day 1 Day 21	IP	20 mg/kg	1x 1x	5 months	8/33 (24) <sup>c</sup> 18/39 (46) <sup>c</sup>	Mesenchymal tumors were most frequent in	
	(VVISIAI)	•	Month 1		30 mg/kg			23/33 (70) <sup>c</sup>	the 3 youngest age	
		al tumors	Month 1.5		30 mg/kg 30 mg/kg	1x 1x		23/33 (70) 5/28 (19) <sup>c</sup>	groups (z test, p <	
			Month 2		30 mg/kg	1x 1x		2/26 (19)	0.001).	
			Month 3		30 mg/kg	1x		3/27 (11) <sup>c</sup>	0.001).	
			Month 4		30 mg/kg	1x		7/32 (22)°		
			Month 5		30 mg/kg	1x		0/14 (0) <sup>c</sup>		
			WOILLIO		50 mg/kg	17		0/17(0)	Continued	nevt nage

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target site	Age when	Dose	Dose	Duration	Age at	Tun	nors	Comments	Reference
	Strain		first dosed	route, # doses		of exposure	death	M	F		
DMN	Rats	Kidney	Day 1	IP	20 mg/kg	1x	5 months	2/33	(6) <sup>c</sup>		Hard, 1979
Dimethyl-	(Wistar)	cortical	Day 21		30 mg/kg	1x			9 (41) <sup>c</sup>		
nitrosamine		epithelial	Month 1		30 mg/kg	1x			3 (36) <sup>c</sup>		
		tumors	Month 1.5		30 mg/kg	1x			3 (52) <sup>c</sup>		
			Month 2		30 mg/kg	1x			(42) <sup>c</sup>		
			Month 3		30 mg/kg	1x			7 (67) <sup>c</sup>		
			Month 4		30 mg/kg	1x		21/32	2 (66) <sup>c</sup> (43) <sup>c</sup>		
	Rats	Total tumors	Month 5	IP	30 mg/kg	1x	≥ 5 months				
	(Wistar)	Total turnors	Day 1 Day 21	IF	20 mg/kg 30 mg/kg	1x 1x	<u>&gt;</u> 5 monus		(33) <sup>c</sup> (64) <sup>c</sup>		
	(Wistai)		Month 1		30 mg/kg	1x			3 (76) <sup>c</sup>		
			Month 1.5		30 mg/kg	1x			3 (63) <sup>c</sup>		
			Month 2		30 mg/kg	1x			5 (50) <sup>c</sup>		
			Month 3		30 mg/kg	1x			7 (67) <sup>c</sup>		
			Month 4		30 mg/kg	1x			2 (69) <sup>c</sup>		
			Month 5		30 mg/kg	1x			(50) <sup>c</sup>		
ENU	Rats	Nervous	Day 1	Injection	20 mg/kg	1x		100	Э% <sup>с</sup>	Susceptibility	Maekawa and
Ethylnitrosourea		system	Day 30	Injection	20 mg/kg	1x		61	% <sup>c</sup>	to neuro-	Mitsumori,
										oncogenic	1990
										effect declined	
										with increasing age.	
	Mice	Liver	Control	Control	None	N/A	90 weeks	1/98	0/96	Both male and	Vesselinovitch,
	(B6C3F <sub>1</sub> )		Castatian	ID	CO/~	4		(1%)	(0%)	female mice	1983
			Gestation	IP	60 μg/g body	1x		28/52	18/49 (37%) <sup>c</sup>	were	
			day 18		•			(54%) <sup>c</sup>	(37%)	responsive to	
			Day 15		weight	1x		41/50	28/51	exposure during prenatal	
			Day 15		60 µg/g body	1.		(82%)°	(55%) <sup>c</sup>	and infant life.	
					weight			(02 /0)	(3370)	and initialit iii6.	
			Day 42		60 µg/g	1x		10/50	5/50		
			Day 12		body	17		(20%) <sup>c</sup>	(10%) <sup>c</sup>		
					weight			(2070)	(1070)		
					- <u>g</u>		•			Continued	next nage

Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species,	Target site	Age when	Dose	Dose	Duration	Age at	Tume	ors	Comments	Reference
	Strain		first dosed	route, # doses		of exposure	death	M	F		
	Rats (Wistar)	Nerve tissue	Control	Control	None	N/A	4-7 months	0/16 (0%)	0/10 (0%)	Highest tumor rate seen when	Naito et al., 1981
	, ,		Gestation day 16	IP	40 mg/kg	1x		26/26 (100%) <sup>c</sup>	18/18 (100 %) <sup>c</sup>	exposed during gestation or soon after birth.	
			Day 1	SC	40 mg/kg	1x		12/12 (100%) <sup>a</sup>	16/16 (100 %) <sup>a</sup>	Statistically significant	
			Week 1		40 mg/kg	1x		12/17 (71%) <sup>c</sup>	18/20 (90%)	decrease in tumor incidence with increasing	
			Week 2		40 mg/kg	1x		10/14 (71%) <sup>c</sup>	14/18 (78%) c	age of exposure.	
			Week 3		40 mg/kg	1x		6/13 (46%) <sup>c</sup>	5/17 (29%)		
			Week 4		40 mg/kg	1x		8/15 (53%) <sup>c</sup>	2/10 (20%)		

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target site	Age	Dose	Dose	Duration of	Age at	Tur	nors	Comments	Reference
	Strain		when first dosed	route, # doses		exposure	death	M	F		
ENU Ethylnitrosourea	Mice (B6C3F <sub>1</sub> )	Lung	Day 1	IP	60 µg/g body	1x		49/55 (89%) <sup>c</sup>	49/50 (98%) <sup>c</sup>		Vesselinovitch et al., 1974
,	,		Day 15		weight	1x		50/55 (91%)°	`47/55 (85%)°		,
			Day 42			1x		53/59 (90%) <sup>c</sup>	44/51 (86%) <sup>c</sup>		
			Day 1		120 µg/g body	1x		36/38 (95%) <sup>c</sup>	54/60 (90%) <sup>c</sup>		
			Day 15		weight	1x		45/49 (92%) <sup>c</sup>	43/50 (86%) <sup>c</sup>		
			Day 42			1x		52/54 (96%) <sup>c</sup>	50/57 (88%) <sup>c</sup>		
	Mice (C3AF1)	Lung	Day 1		60 μg/g body	1x		46/47 (98%) <sup>a</sup>	51/51 (100%) <sup>a</sup>		
	(00/11/)		Day 15		weight	1x		49/49 (100%) <sup>a</sup>	57/59 (97%) <sup>a</sup>		
			Day 42			1x		59/59 (100%) <sup>a</sup>	57/57 (100%) <sup>a</sup>		
			Day 1		120 μg/g body	1x		63/64 (98%) <sup>a</sup>	53/57 (93%) <sup>a</sup>		
			Day 15		weight	1x		54/56 (96%) <sup>a</sup>	50/56 (89%) <sup>a</sup>		
			Day 42			1x		59/59 (100%) <sup>a</sup>	48/48 (100%) <sup>a</sup>		
	Mice (B6C3F <sub>1</sub> )	Liver	Day 1	IP	60 µg/g body	1x		50/54 (93%) <sup>a</sup>	28/43 (65%) <sup>a</sup>		
			Day 15		weight	1x		55/56 (98%) <sup>a</sup>	33/54 (61%) <sup>a</sup>		
			Day 42			1x		12/40 (30%)°	6/39 (15%) <sup>c</sup>		
			Day 1		120 μg/g body	1x		29/34 (85%) <sup>a</sup>	32/53 (60%) <sup>a</sup>		
			Day 15		weight	1x		45/48 (94%) <sup>a</sup>	29/43 (67%) <sup>a</sup>		
			Day 42			1x		`17/49 (35%) <sup>a</sup>	`4/50 (8%) <sup>a</sup>		

Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

cal	Species,	Target site	Age	Dose	Dose	<b>Duration of</b>	Age at	Tun	nors	Comments	Referenc
	Strain		when first dosed	route, # doses		exposure	death	M	F		
	Mice (C3AF <sub>1</sub> )	Liver	Day 1	IP	60 µg/g body	1x		42/45 (93%) <sup>a</sup>	19/41 (46%) <sup>a</sup>		
	(O3Al 1)		Day 15		weight	1x		42/50	19/48		
					· ·			(84%) <sup>a</sup>	(40%) <sup>a</sup>		
			Day 42			1x		7/29 (24%) <sup>c</sup>	4/50		
			Day 1		120 µg/g	1x		(24%) 55/62	(8%) <sup>c</sup> 19/45		
			Day 1		body	17		$(89\%)^a$	(42%) <sup>a</sup>		
			Day 15		weight	1x		35/45	15/35		
								(78%) <sup>a</sup>	(43%) <sup>a</sup>		
			Day 42			1x		8/33 (24%) <sup>c</sup>	3/33 (9%) <sup>c</sup>		
	Mice	Kidney	Day 1	IP	60 µg/g	1x		11/48	5/49		
	(B6C3F <sub>1</sub> )	radioy	Day !		body	174		(23%) <sup>c</sup>	(10%) <sup>c</sup>		
	, ,		Day 15		weight	1x		6/41	7/31		
			D 40			•		(15%) <sup>c</sup>	(23%) <sup>c</sup>		
			Day 42			1x		4/40 (10%) <sup>c</sup>	3/37 (8%) <sup>c</sup>		
			Day 1	120 µg/g	1x		10/30	14/53			
					body			(33%) <sup>a</sup>	(26%) <sup>c</sup>		
			Day 15		weight	1x		17/37	19/49		
			Day 42			4		(46%) <sup>a</sup>	(39%) <sup>c</sup> 11/39		
			Day 42			1x		8/40 (20%) <sup>c</sup>	(28%)°		
	Mice	Kidney	Day 1	ΙP	60 μg/g	1x		7/44	6/45		
	(C3AF1)		Day 15		body	4		(16%) <sup>c</sup>	(13%) <sup>c</sup>		
			Day 15		weight	1x		7/41 (17%) <sup>c</sup>	8/46 (17%) <sup>c</sup>		
			Day 42			1x		3/42	3/43		
			,					(42%) <sup>c</sup>	(7%) <sup>c</sup>		
		***************************************	Day 1		120 μg/g body	1x		4/52 (7%) <sup>c</sup>	6/29 (21%) <sup>a</sup>		
			Day 15	weight	1x		8/35 (23%)°	12/29 (41%) <sup>a</sup>			
			Day 42			1x		6/41 (71%) <sup>c</sup>	`3/39 <sup>°</sup> (8%)°		

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ical	Species,	Target site	Age	Dose	Dose	<b>Duration of</b>	Age at	Tun	nors	Comments	Reference
	Strain		when first dosed	route, # doses		exposure	death	M	F		
	Mice (B6C3F1)	Haderian	Day 1		60 µg/g body	1x		7/40 (17%) <sup>c</sup>	5/43 (12%) <sup>c</sup>		
	,		Day 15		weight	1x		10/51 (20%) <sup>c</sup>	`17/59 (29%)°		
			Day 42			1x		14/50 (28%)°	14/45 (31%) <sup>c</sup>		
		,	Day 1		120 µg/g body	1x		9/30 (30%) <sup>a</sup>	6/52 (12%) <sup>c</sup>		
			Day 15		weight	1x		15/41	8/31 (26%) <sup>c</sup>		
			Day 42			1x		(37%) <sup>a</sup> 25/48 (52%) <sup>a</sup>	(26%) 14/49 (29%) <sup>c</sup>		
	Mice (C3AF1)	Haderian	Day 1		60 μg/g body	1x		3/25 (12%) <sup>c</sup>	4/35 (11%) <sup>c</sup>		
	( /		Day 15		weight	1x		1/9 (11%) <sup>c</sup>	6/38 (16%) <sup>c</sup>		
			Day 42			1x		12/48 (25%) <sup>c</sup>	`5/33 (15%)°		
			Day 1		120 μg/g body	1x		3/52 (6%) <sup>c</sup>	1/25 (4%) <sup>c</sup>		
			Day 15		weight	1x		6/46 (13%) <sup>c</sup>	2/52 (4%) <sup>c</sup>		
			Day 42			1x		`5/29 <sup>°</sup> (17%) <sup>°</sup>	2/11 (18%) <sup>c</sup>		
	Mice (B6C3F1)	Stomach	Day 1		60 µg/g body	1x		3/48 (6%) <sup>c</sup>	4/43 (9%) <sup>c</sup>		
	, ,		Day 15		weight	1x		10/42 (24%) <sup>a</sup>	7/45 (16%) <sup>c</sup>		
			Day 42			1x		9/51 (18%) <sup>a</sup>	8/36 (22%) <sup>c</sup>		
		•	Day 1		120 µg/g body	1x		2/29 (7%) <sup>c</sup>	9/53 (17%) <sup>c</sup>		
			Day 15		weight	1x		10/35 (29%) <sup>a</sup>	12/33 (36%) <sup>c</sup>		
			Day 42			1x		12/53 (23%) <sup>a</sup>	12/50 (24%) <sup>c</sup>		

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Chemical	Species, Strain	Target site	Age when	Dose route,	Dose	Duration of exposure	Age at death	Tun	nors	Comments	Reference	
	Strain		first dosed	# doses		exposure	ueatii	M	F			
	Mice (C3AF1)	Stomach	Day 1		60 µg/g body	1x		2/39 (5%) <sup>c</sup>	7/45 (16%) <sup>c</sup>			
	,		Day 15		weight	1x		7/45 (16%) <sup>a</sup>	7/38 (18%) <sup>c</sup>			
			Day 42			1x		14/55 (25%) <sup>a</sup>	7/49 (14%)°			
			Day 1		120 μg/g	1x		8/60	9/44	п		
			Day 15		body weight	1x		(13%) <sup>c</sup> 16/51	(20%) <sup>c</sup> 11/42			
			Day 42			1x		(31%) <sup>a</sup> 19/48	(26%) <sup>c</sup> 13/37			
	Mice	Malignant	Day 1		60 μg/g	1x		(40%) <sup>a</sup> 2/55	(35%) <sup>c</sup> 6/52			
	(B6C3F1)	Lymphomas 	Day 15		body weight	1x		(4%) <sup>c</sup> 3/56	(12%) <sup>a</sup> 14/59			
			Day 42			1x		(5%) <sup>c</sup> 9/59	(24%) <sup>a</sup> 17/59			
				Day 1		120 μg/g	1x		(15%) <sup>c</sup> 8/39	(29%) <sup>a</sup> 15/65		
			Day 15		body weight	1x		(20%) <sup>c</sup> 14/60	(23%) <sup>a</sup> 17/58			
				Day 42			1x		(23%) <sup>c</sup> 12/59	(29%) <sup>a</sup> 14/60		
	Mice	Malignant	Day 1		60 µg/g	1x		(20%) <sup>c</sup> 6/49	(23%) <sup>a</sup> 8/49			
	(C3AF1)	Lymphomas	Day 15		body weight	1x		(12%) <sup>c</sup> 3/49	(16%) <sup>a</sup> 13/61			
			Day 42		Weight	1x		(6%) <sup>c</sup> 6/60	(21%) <sup>a</sup> 9/55			
			-		400/			(10%) <sup>c</sup>	(16%) <sup>a</sup>			
			Day 1		120 µg/g body	1x		3/66 (5%) <sup>c</sup>	10/58 (17%) <sup>a</sup>			
			Day 15		weight	1x		10/56 (18%) <sup>c</sup>	18/60 (30%) <sup>a</sup>			
			Day 42			1x		3/49 (6%) <sup>c</sup>	13/50 (26%) <sup>a</sup>			

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species, Strain	Target Site	Age when	Dose Route, #	Dose	Duration of exposure	Age at death		mor lence	Comments	Reference
			first dosed	doses				M	F		
NMU N-nitroso-	Mice (BC3F1)	Total tumors	Control	Control	N/A	N/A	60 weeks	1/20 (5%)	0%	Control mice did not exhibit	Terracini and Testa, 1970
methylurea	, ,	Lung	Day 1	IP	50 μg/g body weight	1x	60 weeks	12/15 (80%)°	16/19 (84%) <sup>c</sup>	tumors in target sites except a single hepatoma	
			5 weeks		50 µg/g body weight	1x	60 weeks	10/26 (39%)°	10/35 (29%) <sup>c</sup>	in a male control mouse	
		Lympho- sarcoma	Day 1		50 μg/g body weight	1x	60 weeks	23/39 (59%) <sup>c</sup>	23/45 (51%) <sup>c</sup>		
		***************************************	5 weeks		50 μg/g body weight	1x	60 weeks	11/35 (31%) <sup>c</sup>	21/45 (47%) <sup>c</sup>		
		Liver	Day 1		50 μg/g body weight	1x	60 weeks	10/12 (83%) <sup>c</sup>	1/17 (6%) <sup>c</sup>		
			5 weeks		50 µg/g body weight	1x	60 weeks	0% <sup>c</sup>	0% <sup>b</sup>		
		Kidney	Day 1		50 µg/g body weight	1x	60 weeks	3/15 (20%) <sup>c</sup>	3/18 (17%) <sup>c</sup>		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/21 (10%) <sup>c</sup>	0% <sup>b</sup>		
		Fore- stomach	Day 1		50 μg/g body weight	1x	60 weeks	0% <sup>c</sup>	4/17 (24%) <sup>c</sup>		
			5 weeks		50 μg/g body weight	1x	60 weeks	8/22 (36%) <sup>c</sup>	12/18 (67%) <sup>c</sup>	0 "	
										Continue	ed next page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species, Strain	Target Site	Age when	Dose Route, #	Dose	Duration of exposure	Age at death		mor lence	Comments	Reference
			first dosed	doses				M	F		
NMU N-nitroso-	Rats (Wistar)	Mammary	Day 1	IP	50 µg/g body weight	1x	60 weeks	0% <sup>c</sup>	4/14 (29%) <sup>c</sup>	Tumor incidence for control rats	Terracini and Testa, 1970
methylurea	,		5 weeks		50 μg/g body weight	1x	60 weeks	0% <sup>c</sup>	3/5 (60%) <sup>c</sup>	was based on previous experiments	
		Lympho- sarcoma	Day 1		50 μg/g body weight	1x	60 weeks	1/10 (10%) <sup>c</sup>	0% <sup>c</sup>	(Della Porta et al., 1968) and	
			5 weeks		50 μg/g body weight	1x	60 weeks	2/8 (25%) <sup>c</sup>	1/11 (9%) <sup>c</sup>	was not specifically reported in this	
		Kidney (Ana- plastic)	Day 1		50 μg/g body weight	1x	60 weeks	14/18 (78%) <sup>c</sup>	9/13 (69%) <sup>c</sup>	paper	
			5 weeks		50 μg/g body weight	1x	60 weeks	2/5 (40%) <sup>c</sup>	5/12 (42%) <sup>c</sup>		
		Kidney (Adenoma)	Day 1		50 μg/g body weight	1x	60 weeks	3/14 (21%) <sup>c</sup>	2/6 (33%) <sup>c</sup>		
			5 weeks		50 μg/g body weight	1x	60 weeks	1/4 (25%) <sup>c</sup>	0% <sup>c</sup>		
		Fore- stomach	Day 1		50 μg/g body weight	1x	60 weeks	4/14 (29%) <sup>c</sup>	3/6 (50%) <sup>c</sup>		
			5 weeks		50 µg/g body weight	1x	60 weeks	0% <sup>c</sup>	0% <sup>c</sup>		
		Intestine	Day 1		50 μg/g body weight	1x	60 weeks	3/10 (30%)°	2/2 (100%) <sup>c</sup>		
			5 weeks		50 µg/g body weight	1x	60 weeks	2/4 (50%) <sup>c</sup>	0% <sup>c</sup>	<b>0</b>	d novt nago

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors

Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species, Strain	Target Site	Age when	Dose Route, #	Dose	Duration of exposure	Age at death*		mor lence	Comments	Reference
			first dosed	doses				M	F		
NMU N-nitroso- methylurea	Mice (C3Hf/Dp)	Thymus	Day 1 Day 1 Day 1 Day 21 Day 70	IΡ	NA  25 µg NMU/g bodyweight  25 µg NMU/g bodyweight  50 µg NMU/g bodyweight  50 µg NMU/g bodyweight  50 µg NMU/g	NA 1x 1x 1x 1x	120 wks  29 ± 8.4	0/34 (0%) 2/16 (13%)° 0/20 (0%)b 16/24 (67%)° 14/44 (32%)°	0/25 (0%) 5/25 (20%)° 1/20 (5%)° 30/44 (68%)° 18/38 (47%)° 6/41 (15%)°	Age at death from thymic lymphoma reported specifically for some, but not all, dose groups.  Control mice were sacrificed at 120 wks  Age of death for all mice in this dose group, regardless of cancer type	Terracini et al., 1976
					bodyweight					0 "	

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Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species,	Target	Age when	Dose	Dose	Duration	Age a	t death	Tumor I	ncidence	Reference
	Strain	Site	first dosed	Route, # doses		of exposure	M	F	M	F	
NMU N-nitroso- methylurea	Mice (C3Hf/Dp)	Extra- thymic lymphoma	control	IP	NA	NA	120 weeks	120 weeks	1/34 (3%)	2/25 (8%)	Terracini et al., 1976
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	2/16 (13%) <sup>c</sup>	1/25 (4%) <sup>c</sup>	
			Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	0/20 (0%) <sup>c</sup>	0/20 (0%) <sup>c</sup>	
			Day 1		50 μg NMU/g bodyweight	1x	70 weeks	80 weeks	0/24 (0%) <sup>c</sup>	0/44 (0%) <sup>c</sup>	
			Day 21		50 μg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%) <sup>c</sup>	0/38 (0%) <sup>c</sup>	
			Day 70		50 μg NMU/g bodyweight	1x	110 weeks	90 weeks	1/30 (3%) <sup>c</sup>	0/41 (0%) <sup>c</sup>	
		Lung	control	IP	NA	NA	120 weeks	120 weeks	4/34 (12%)	6/25 (24%)	
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	7/16 (44%) <sup>c</sup>	13/25 (52%) <sup>c</sup>	
			Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	12/20 (60%) <sup>c</sup>	8/20 (40%) <sup>c</sup>	
			Day 1		50 μg NMU/g bodyweight	1x	70 weeks	80 weeks	5/24 (21%) <sup>c</sup>	11/44 (25%) <sup>c</sup>	
			Day 21		50 μg NMU/g bodyweight	1x	100 weeks	90 weeks	23/44 (52%) <sup>c</sup>	15/38 (39%) <sup>c</sup>	
			Day 70		50 μg NMU/g bodyweight	1x	110 weeks	90 weeks	18/30 (60%) <sup>c</sup>	24/41 (59%) <sup>c</sup>	Continued next

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Chemical	Species, Strain	Target Site	Age when	Dose Route,	Dose	Duration of exposure	Age a	t death		mor lence	Reference
			first dosed	# doses			M	F	M	F	
NMU N-nitroso- methylurea	Mice (C3Hf/Dp)	Liver	control	IP	NA	NA	120 weeks	120 weeks	13/34 (38%)	1/25 (4%)	Terracini et al., 1976
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	9/16 (56%) <sup>a</sup>	2/25 (8%) <sup>c</sup>	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	12/20 (60%) <sup>a</sup>	2/20 (10%) <sup>c</sup>	
			Day 1		50 μg NMU/g bodyweight	1x	70 weeks	80 weeks	4/24 (17%) <sup>a</sup>	3/44 (7%) <sup>c</sup>	
			Day 21		50 μg NMU/g bodyweight	1x	100 weeks	90 weeks	21/44 (48%) <sup>a</sup>	1/38 (2.6%) <sup>c</sup>	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	8/30 (27%) <sup>a</sup>	2/41 (5%) <sup>c</sup>	
		Stomach	control	IP	NA	NA	120 weeks	120 weeks	0/34 (0%)	5/25 (20%)	-
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	2/16 (13%) <sup>c</sup>	10/25 (40%) <sup>c</sup>	
			Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	3/20 (15%) <sup>c</sup>	7/20 (35%) <sup>c</sup>	
			Day 1		50 μg NMU/g bodyweight	1x	70 weeks	80 weeks	2/24 (8%) <sup>c</sup>	1/44 (2%) <sup>c</sup>	
			Day 21		50 μg NMU/g bodyweight	1x	100 weeks	90 weeks	19/44 (43%) <sup>c</sup>	9/38 (24%) <sup>c</sup>	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	8/30 (27%) <sup>c</sup>	21/41 (51%) <sup>c</sup>	

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age a	t death	Tumor Ir	ncidence	Reference
	Strain	Site	when first dosed	Route, # doses		exposure	M	F	М	F	
NMU N-nitroso- methylurea	Mice (C3Hf/Dp)	Kidney	control	IP	NA	NA	120 weeks	120 weeks	0/34 (0%)	0/25 (0%)	Terracini et al., 1976
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	0/16 (0%) <sup>c</sup>	0/25 (0%) <sup>c</sup>	
			Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	0/20 (0%) <sup>c</sup>	0/20 (0%) <sup>c</sup>	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	0/24 (0%) <sup>c</sup>	4/44 (9%) <sup>c</sup>	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%) <sup>c</sup>	4/38 (11%) <sup>c</sup>	
			Day 70		50 µg NMU/g bodyweight	1x	110 weeks	90 weeks	5/30 (17%) <sup>c</sup>	7/41 (17% ) <sup>c</sup>	
		Ovary	control	IP	NA	NA	120 weeks	120 weeks	NA	3/25 (12%)	
			Day 1		25 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	2/25 (8%) <sup>c</sup>	
			Day 70		25 µg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	4/20 (20%) <sup>c</sup>	
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%) <sup>c</sup>	
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	9/38 (24%) <sup>c</sup>	
			Day 70		50 μg NMU/g bodyweight	1x	110 weeks	90 weeks	NA	16/41 (39%) <sup>c</sup>	Continued next page

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Chemical	Species,	Target	Age	Dose	Dose	Duration of	Age a	t death	Tumor	Incidence	Reference	
	Strain	Site	when first dosed	Route, # doses		exposure	M	F	M	F		
NMU N-nitroso- methylurea	Mice (C3Hf/Dp)	Mammary	control	IP	NA	NA	120 weeks	120 weeks	NA	2/25 (8%)	Terracini et al., 1976	
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/25 (4%) <sup>c</sup>		
			Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	0/20 (0%) <sup>c</sup>		
			Day 1		50 µg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%) <sup>c</sup>		
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	1/44 (2%) <sup>c</sup>	0/38 (0%) <sup>c</sup>		
			Day 70		50 µg NMU/g bodyweight		110 weeks	90 weeks	NA	4/41 (9.8%) <sup>c</sup>		
		Uterus or Vagina	control	IP	NA	NA	120 weeks	120 weeks	NA	1/25 (4%)		
			Day 1		25 μg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/25 (4%) <sup>c</sup>		
			Day 70	Day 70		25 μg NMU/g bodyweight	1x	120 weeks	100 weeks	NA	6/20 (30%) <sup>c</sup>	
			Day 1		50 μg NMU/g bodyweight	1x	70 weeks	80 weeks	NA	0/44 (0%) <sup>c</sup>		
			Day 21		50 µg NMU/g bodyweight	1x	100 weeks	90 weeks	NA	1/38 (3%) <sup>c</sup>		
			Day 70		50 µg NMU/g bodyweight		110 weeks	90 weeks		7/41 (17%) <sup>c</sup>	Continued, next page	

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Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species,	Target	Age when	Dose	Dose	Duration of	Age at death	Tur	nors	Comments	Reference
	Strain	site	first dosed	route, # doses		exposure		M	F		
Urethane	Mice (SWR)	Lung adenoma	Newborn	SC	0.18 mg/g body weight	1x	10 weeks	100		The average number of	Kaye and Trainin, 1966
			11-22 weeks	SC	0.25 mg/g body weight	1x	23-34 weeks	0%	<sup>℃</sup>	tumors per mouse increased linearly with dose.	
	Mice (C3H/f)	Liver	Control	Control	None	N/A	493 days (m) 553 days (f)	14/97 (14%)	1/77 (1%)		Liebelt et al., 1964
	(== - )		Day 1	IP	0.8 mg/g body weight	1x	481 days (m) 434 days (f)	27/30 (90%) <sup>a</sup>	18/39 (46%) <sup>a</sup>		
			8-10 weeks	IP	1 mg/g body weight	1x	321 days (m)	6/25 (24%) <sup>b</sup>	0/32 (0%) <sup>b</sup>		
		Lung	Control	Control	None	N/A	493 days (m) 553 days (f)	0/97 (0%)	0/77 (0%)	The number of lung tumors	•
			Day 1	IP	0.8 mg/g body weight	1x	401 days (m) 408 days (f)	14/30 (46%) <sup>a</sup>	19/39 (48%) <sup>a</sup>	among the controls was not	
			8-10 weeks	IP	1 mg/g body weight	1x	506 days (m) -	2/25 (8%) <sup>b</sup>	0/32 (0%) <sup>b</sup>	provided.	_
		Reticular tissue	Control	Control	None	N/A	493 days (m) 553 days (f)	2/97 (2%)	6/77 (8%)		
			Day 1	IP	0.8 mg/g body weight	1x	285 days (m) 343 days (f)	4/30 (13%) <sup>b</sup>	22/39 (56%) <sup>a</sup>		
			8-10 weeks	IP	1 mg/g body weight	1x	- 453 days (f)	0/25 (25%) <sup>b</sup>	4/32 (13%) <sup>b</sup>		••••••••••••••••••••••••••••••••
	Mice (Swiss)	Leukemia	Control Day 1	Control SC	None 2 mg in 0.05 ml aqueous solution	N/A 1x	8-10 months	19 13/ (22)	60	Highest tumor rates when dosed at birth.	Fiore-Donati et al., 1962
			Day 5		4 mg in 0.05 ml aqueous solution	1x		7/3 (18 <sup>9</sup>	%) <sup>c</sup>	Exposure to newborns was followed by	
			Day 40		20 mg in 0.1 ml aqueous solution	1x		2/6 (3%		21.6% leukemia, occurring at a mean age of 105 days.  Continued, ne	ext page

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species,	Target	Age	Dose	Dose	<b>Duration of</b>	Age at	Tumo	rs	Comments	Reference
	Strain	site	when first dosed	route, # doses		exposure	death	M	F		
Urethane	Mice (Swiss)	Lung adenoma	Control 2 weeks	Control	None	N/A	9 weeks	0/15 (0%)	-	The proportion of animals with	Rogers, 1951
	,		Control 4 weeks	Control	None	N/A	11 weeks	0/14 (0%)	-	adenomas decreased	
			Control 6 weeks	Control	None	N/A	13 weeks	1/15 (7%)	-	steadily with age of	
			Control 8 weeks	Control	None	N/A	15 weeks	2/15 (13%)	-	exposure.	
			Control 10 weeks	Control	None	N/A	17 weeks	0/15 (0%)	-		
			2 weeks	IP	1 mg/g body weight	1x	9 weeks	24/24 (100%) <sup>c</sup>	-		
			4 weeks	IP	1 mg/g body weight	1x	11 weeks	23/25 (92%) <sup>c</sup>	-		
		Lung ) adenoma	6 weeks	IP	1 mg/g body weight	1x	13 weeks	`22/25 (88%)°	-		
			8 weeks	IP	1 mg/g body weight	1x	15 weeks	21/25 (84%) <sup>c</sup>	-		
			10 weeks	IP	1 mg/g body weight	1x	17 weeks	19/25 (76%) <sup>c</sup>	-		
	Mice (Swiss)		3 weeks	IP	0.25 mg/g body weight	1x	12 weeks	16/19 (84%) <sup>c</sup>	-	ин <b>и</b>	
					0.5 mg/g body weight	1x	12 weeks	16/20 (80%) <sup>c</sup>	-		
					1 mg/g body weight	1x	12 weeks	18/20 (90%) <sup>c</sup>	-		
			8 weeks	IP	0.25 mg/g body weight	1x	17 weeks	4/17 (24%) <sup>c</sup>	-		
					0.5 mg/g body weight	1x	17 weeks	15/16 (94%) <sup>c</sup>	-		
					1 mg/g body weight	1x	17 weeks	`18/18 (100%) <sup>c</sup>	-		
					J			, ,		Continue	ance type he

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Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species, Strain	Target Site	Age when	Dose Route,	Dose	Duration of exposure	Age at death	Tumor In	cidence	Comments	Reference
			first dosed	# doses				M	F		
Urethane	Mice (Swiss)	liver	Control	Control	N/A	N/A	360-720 days	10/227 (4.4%)	4/222 (8.22%)		Chieco-Bianchi et al., 1963
	, ,		Day 1	SC	1 mg/g body weight	1x	180 days	1/20 (5%) <sup>a</sup>	0/20 (0%) <sup>b</sup>		
			Day 1	SC	1 mg/g body weight	1x	240 days	2/17 (12%) <sup>a</sup>	0/12 (0%) <sup>b</sup>		
			Day 1	SC	1 mg/g body weight	1x	300 days	5/18 (28%) <sup>a</sup>	0/16 (0%) <sup>b</sup>		
			Day 1	SC	1 mg/g body weight	1x	360 days	11/20 (55%) <sup>a</sup>	0/23 (0%) <sup>b</sup>		
			Day 1	SC	1 mg/g body weight	1x	420 days	13/15 (87%) <sup>a</sup>	2/22 (9%) <sup>a</sup>		
			Day 1	SC	1 mg/g body weight	1x	480 days	17/23 (74%) <sup>b</sup>	2/25 (8%) <sup>b</sup>		
			Day 5	SC	1 mg/g body weight	1x	420 days	9/13 (69.2%) <sup>c</sup>	2/11 (18.2%)		
			Day 20	SC	1 mg/g body weight	1x	420 days	1/13 (8%) <sup>c</sup>	0/16 (0%) <sup>c</sup>		
			Day 40	SC	1 mg/g body weight	1x	420 days	0/11 (0%) <sup>c</sup>	0/9 (0%) <sup>c</sup>		
Urethane	Mice	skin	Control	Control	N/A	N/A	180-550 days	30/7		Croton oil treatment	Chieco-Bianchi et al., 1963
	(Swiss)							(4.21		initiated at 40	et al., 1909
			Day 1	SC	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2x/week for 10 mos	660 days	26/5 (44.1	%) <sup>a</sup>	days of age	
			Day 40	SC	1 mg urethane/g body weight; 5% croton oil	single dose urethane, croton oil applied 2x/week for 10 mos	700 days	8/4 (19.5			

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Chemical	Species, Strain	Target Site	Age when first dosed	Dose Route, # doses	Dose	Duration of exposure	Age at death	Tumor In	cidence F	Comments	Reference
Urethane	Mice (B6AF1/J)	Liver	Control	gavage	N/A	N/A	71 weeks	1/25 (4%)	0/25 (0%)		Klein, 1966
	,		Day 1		1 mg/g body weight	1x	66 weeks	9/20 (45%) <sup>a</sup>	9/26 (35%) <sup>a</sup>		
			Day 7		1 mg/g body weight	1x	67 weeks	20/22 (91%) <sup>a</sup>	20/26 (77%) <sup>a</sup>		
			Day 14		1 mg/g body weight	1x	68 weeks	16/20 (80%) <sup>a</sup>	10/23 (43%) <sup>a</sup>		
			Day 21		1 mg/g body weight	1x	69 weeks	13/23 (57%) <sup>a</sup>	1/20 (5%) <sup>a</sup>		
			Day 28		1 mg/g body weight	1x	70 weeks	4/24 (17%) <sup>a</sup>	1/20 (5%) <sup>a</sup>		
		Lung	Control	gavage	1 mg/g body weight	1x	71 weeks	9/25 (36%)	6/25 (24%)		
			Day 1		1 mg/g body weight	1x	66 weeks	20/20 (100%)°	25/26 (96%) <sup>c</sup>		
			Day 7		1 mg/g body weight	1x	67 weeks	22/22 (100%) <sup>c</sup>	26/26 (100%) <sup>c</sup>		
			Day 14		1 mg/g body weight	1x	68 weeks	19/20 (95%) <sup>c</sup>	19/23 (83%) <sup>c</sup>		
			Day 21		1 mg/g body weight	1x	69 weeks	23/23 (100%) <sup>c</sup>	19/20 (95%) <sup>c</sup>		
			Day 28		1 mg/g body weight	1x	70 weeks	24/24 (100%) <sup>c</sup>	20/20 (100%) <sup>c</sup>		

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

Barton, H., et al.: Assessing Susceptibility from Early-Life Exposure to Carcinogens

Chemical	Species, Strain	Target Site	Age when	Dose Route,	Dose	Duration of	Age at death	Tur Incid		Comments	Reference
			first dosed	# doses		exposur e		M	F		
Urethane	Mice (B6AF1/J)	Harderian gland	Control	gavage	1 mg/g body weight	1x	71 weeks	0/25 (0%)	0/25 (0%)		Klein, 1966
	,		Day 1		1 mg/g body weight	1x	66 weeks	0/20 (0%) <sup>b</sup>	1/26 (4%) <sup>c</sup>		
			Day 7		1 mg/g body weight	1x	67 weeks	0/22 (0%) <sup>b</sup>	1/26 (4%) <sup>c</sup>		
			Day 14		1 mg/g body weight	1x	68 weeks	0/20 (0%) <sup>b</sup>	2/23 (9%) <sup>c</sup>		
			Day 21		1 mg/g body weight	1x	69 weeks	1/23 (4%) <sup>c</sup>	0/20 (0%) <sup>b</sup>		
			Day 28		1 mg/g body weight	1x	70 weeks	0/24 (0%) <sup>b</sup>	0/20 (0%) <sup>b</sup>		
		Fore- stomach	Control	gavage	1 mg/g body weight	1x	71 weeks	0/25 (0%)	1/25 (4%)		
			Day 1		1 mg/g body weight	1x	66 weeks	0/20 (0%) <sup>b</sup>	3/26 (12%) <sup>c</sup>		
			Day 7		1 mg/g body weight	1x	67 weeks	1/22 (5%) <sup>c</sup>	1/26 (4%) <sup>c</sup>		
			Day 14		1 mg/g body weight	1x	68 weeks	1/20 (5%) <sup>c</sup>	4/23 (17%) <sup>c</sup>		
			Day 21		1 mg/g body weight	1x	69 weeks	0/23 (0%) <sup>b</sup>	1/20 (5%) <sup>c</sup>		
			Day 28		1 mg/g body weight	1x	70 weeks	2/24 (8%) <sup>c</sup>	1/20 (5%) <sup>c</sup>		

a) significant compared to controls; b) evaluated but not significant compared to controls; c) not evaluated by authors.

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Supplementary Table 3. Ratio of early-life to adult cancer potencies for studies with acute exposures of juveniles and adult animals to mutagenic chemicals.

J						Ratio of	f Juvenile	to Adult Po	tency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
BaP*	Mice	male	75 μg/kg	liver	1 day	9.3	2.9	8.4	55	Vesselinovitch et al., 1975a
	(B6C3F1)				15 days	11	3.5	9.6	61	
		female	75 µg/kg		1 day	1.2	0.0083	1.6	31	
					15 days	1.7	0.015	2.1	36	
		male	150 µg/kg		1 day	29	8.2	26	194	
					15 days	15	4.1	13	109	
		female	150 μg/kg		1 day	8.8	1.4	8.1	94	
					15 days	1.2	0.0082	1.6	30	
	Mice	male	75 µg/kg	liver	1 day	11	2.1	10	112	10
	(C3AF1)				15 days	7.5	1.1	7.0	83	
		female	75 µg/kg		1 day	0.2	0.0018	0.26	9.1	
					15 days	0.2	0.0017	0.24	8.5	
		male	150 µg/kg		1 day	14	3.0	12.8	130	
					15 days	3.6	0.11	3.8	49	
		female	150 µg/kg		1 day	0.21	0.0017	0.24	8.8	
					15 days	0.20	0.0017	0.24	8.7	
	Mice	male	75 µg/kg	lung	1 day	1.2	0.45	1.2	3.4	
	(B6C3F1)				15 days	0.22	0.0046	0.31	1.4	
		female	75 µg/kg	lung	1 day	2.8	1.1	2.7	9.5	
					15 days	1.4	0.41	1.4	5.1	
		male	150 µg/kg	lung	1 day	2.2	1.0	2.1	5.4	
					15 days	0.79	0.2	0.82	2.3	
		female	150 μg/kg	lung	1 day	7.9	2.6	7.2	43	
				***************************************	15 days	3.7	1.1	3.4	22	

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						Ratio o	f Juveni	ile to Adult	Potency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
BaP* (cont.)	Mice	male	75 µg/kg	lung	1 day	1.2	0.47	1.2	3.2	
	(C3AF1)				15 days	1.1	0.43	1.1	3.1	
		female	75 μg/kg	lung	1 day	1.6	0.66	1.6	4.0	
					15 days	1.6	0.71	1.6	4.2	
		male	150 µg/kg	lung	1 day	1.5	0.57	1.5	5.0	
					15 days	1.9	0.71	1.8	6.0	
		female	150 µg/kg	lung	1 day	1.3	0.61	1.3	2.9	
					15 days	1.2	0.54	1.1	2.6	
DBA	Mice			lung		178	20	143	5100	Law, 1940
DEN**	Mice	male	6 μg/kg	liver	1 day	9.0	3.5	8.3	37	Vesselinovitch et al., 1984
	(B6C3F1)				15 days	8.9	3.5	8.2	36	
		female	6 μg/kg	liver	1 day	35	9.1	31	239	
					15 days	25	6.3	226	175	
		male	12 μg/kg	liver	1 day	9.6	3.3	8.8	50	
					15 days	9.8	3.4	8.9	51	
		female	12 μg/kg	liver	1 day	16	5.9	15	67	
					15 days	19	7.1	18	79	
	Mice	Male	6 μg/kg	liver	1 day	7.3	2.9	6.9	26	
	(C3AF1)				15 days	3.5	1.4	3.3	13	
		female	6 μg/kg	liver	1 day	17	3.2	16	166	
					15 days	6.4	0.86	6.0	73	
		Male	12 µg/kg	liver	1 day	11	3.7	9.5	53	
					15 days	9.8	3.4	8.9	50	
		female	12 μg/kg	liver	1 day	40	8.5	36	340	
					15 days	25	5.0	22	221	

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		.,				Ratio of	Juvenile	to Adult Po	otency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
DEN** (cont.)	Mice	male	6 µg/kg	lung	1 day	0.51	0.27	0.52	0.93	Vesselinovitch et al., 198
	(B6C3F1)				15 days	1.6	0.95	1.6	2.7	
		female	6 µg/kg	lung	1 day	0.89	0.54	0.89	1.5	
					15 days	1.2	0.76	1.2	2.0	
		male	12 µg/kg	lung	1 day	0.40	0.21	0.40	0.73	
					15 days	0.66	0.39	0.66	1.1	
		female	12 µg/kg	lung	1 day	0.72	0.44	0.73	1.2	
					15 days	1.4	0.88	1.4	2.3	
	Mice	male	6 µg/kg	lung	1 day	0.66	0.22	0.67	1.7	
	(C3AF1)				15 days	0.54	0.21	0.56	1.3	
		female	6 µg/kg	lung	1 day	1.1	0.45	1.1	2.5	
					15 days	0.74	0.36	0.74	1.5	
		male	12 μg/kg	lung	1 day	0.31	0.084	0.33	0.76	
					15 days	0.61	0.26	0.62	1.4	
		female	12 μg/kg	lung	1 day	0.75	0.35	0.75	1.6	
					15 days	0.75	0.37	0.75	1.5	
DMBA <sup>#</sup>	Rats	male		total	2v5-8 wks	3.3	1.3	3.2	10	Meranze et al., 1969
	(Wistar)				2v26 wks	3.2	1.3	3.1	9.7	
		female		total	2v5-8 wks	1.3	0.68	1.3	2.5	
					2v26 wks	3.3	1.2	3.0	16	
				mammary	2v5-8 wks	0.041	0.0012	0.056	0.26	
					2v26 wks	0.22	0.0023	0.29	5.3	
					5v26 wks	7.1	1.8	6.4	55	
•	Mice	male	15 µg	lung	1 day	30	2.8	22	1482	Walters, 1966
	(Balb/c)				15-19 days	1.0	0.28	1.0	3.5	
		male	30 µgx2	lung	15-19 days	14	1.1	10	978	
		female	15 µg	lung	1 day	•		46	2350	
			. 0	lulig	15-19 days	3.1	0.51	3.0	22	
		female	30 µgx2	lung	15-19 days	15	1.2	11	1004	
•	Mice			lymphoma	-	2.7	0.60	2.5	19	Pietra et al., 1961
	(Swiss)			lung		9.1	2.9	8.7	40	

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						Ratio of	Juvenile	to Adult Po	otency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
DMN***	Rats		3 wks	total	1 month	0.73	0.41	0.73	1.3	Hard, 1979
	(Wistar)				1.5 months	1.1	0.58	1.1	2.1	
					2 months	1.5	0.75	1.5	3.0	
					3 months	0.94	0.50	0.94	1.8	
			24 hr		1 month	0.28	0.13	0.28	0.6	
					1.5 months	0.42	0.18	0.42	0.9	
					2 months	0.56	0.24	0.56	1.3	
					3 months	0.36	0.16	0.36	0.78	
			1 month		1.5 months	1.5	0.80	1.5	3.0	
					2 months	2.0	1.0	2.0	4.2	
					3 months	1.3	0.69	1.3	2.5	
ENU	Mice	male		liver		7.8	3.9	7.7	18	Vesselinovitch, 1983
	(B6C3F1)	female				7.1	2.9	6.9	21	
	Rats	male		nerve tissue	1 day	27	2.5	20	1374	Naito et al., 1981
	(Wistar)				1 week	1.6	0.61	1.6	4.6	
					2 weeks	1.6	0.58	1.6	4.8	
					3 weeks	0.68	0.12	0.72	2.3	
		female			1 day	64	6.0	50	2488	
					1 weeks	9.6	2.6	8.9	59	
					2 weeks	6.2	1.6	5.7	40	
					3 weeks	0.69	0.0090	0.89	8.9	
	Mice	male	60 μg/g	lung	1	1.0	0.60	1.0	1.7	Vesselinovitch et al., 1974
	(B6C3F1)				15	1.1	0.66	1.1	1.8	
		female	60 μg/g	lung	1	2.1	1.17	2.1	4.1	
					15	1.0	0.60	1.0	1.7	
		male	120 μg/g	lung	1	1.0	0.60	1.0	1.7	
					15	1.1	0.66	1.0	1.8	
		female	120 μg/g	lung	1	2.1	1.2	2.1	4.1	
					15	1.0	0.60	1.0	1.7	

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						Ratio of	Juvenile	to Adult P	otency	
ompound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
NU (cont.)	Mice	male	60 µg/g	lung	1	8.7	2.7	8.0	48	
	(C3AF1)				15	52	5.2	39	2141	
		female	60 µg/g	lung	15	0.71	0.32	0.72	1.6	
		male	120 µg/g	lung	1	0.92	0.38	0.92	2.2	
					15	0.67	0.28	0.67	1.6	
		female	120 µg/g	lung	1	0.54	0.24	0.54	1.2	
					15	0.42	0.18	0.42	0.92	
	Mice	male	60 µg/g	liver	1	8.8	4.2	8.5	22	
	(B6C3F1)				15	14	6.2	14	37	
		female	60 µg/g	liver	1	6.3	2.6	6.1	18	
					15	5.6	2.4	5.4	16	
	Mice-	male	120 µg/g	liver	1	5.2	2.5	5.1	11	
					15	7.6	3.9	7.5	17	
		female	120 µg/g	liver	1	11	4.1	11	46	
					15	14	4.9	13	55	
		male	60 µg/g	liver	1	12	4.7	11	43	
	(C3AF1)				15	8.1	3.2	7.6	29	
		female	60 µg/g	liver	1	7.5	2.6	7.0	32	
					15	4.8	1.8	4.6	18	
		male	120 µg/g	liver	1	9.8	4.1	9.3	32	
					15	6.6	2.7	6.3	23	
		female	120 µg/g	liver	1	5.4	1.7	5.0	25	
					15	5.4	1.7	5.1	25	
	Mice	male	60 µg/g	kidney	1	2.2	0.73	2.1	8.0	
	(B6C3F1)			-	15	1.2	0.29	1.2	5.1	
		female	60 µg/g	kidney	1	0.72	0.024	0.85	5.9	
					15	2.6	0.61	2.5	15	
		male	120 µg/g	kidney	1	1.7	0.65	1.7	4.4	
				-	15	2.6	1.1	2.6	6.4	
		female	120 µg/g	kidney	1	0.87	0.37	0.87	2.0	
					15	1.4	0.67	1.4	3.2	

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							Juvenile	to Adult Po	otency	
ompound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs
NU (cont.)	Mice	male	60 µg/g	kidney	1	1.8	0.17	1.9	15	
	(C3AF1)				15	2.0	0.25	2.0	16	
		female	60 µg/g	kidney	1	1.0	0.016	1.3	13	
					15	2.1	0.16	2.2	20	
		male	120 µg/g	kidney	1	0.17	0.0029	0.24	1.5	
					15	1.5	0.38	1.5	5.9	
		female	120 µg/g	kidney	1	2.3	0.17	2.4	20	
					15	7.1	1.8	6.5	47	
	Mice	male	60 µg/g	Harderian	1	0.34	0.018	0.41	1.4	
	(B6C3F1)				15	0.48	0.075	0.52	1.4	
		female	60 µg/g	Harderian	1	0.11	0.0025	0.16	0.74	
					15	0.84	0.35	0.84	2.0	
		male	120 µg/g	Harderian	1	0.41	0.13	0.42	0.96	
					15	0.57	0.26	0.57	1.2	
		female	120 μg/g	Harderian	1	0.13	0.0030	0.18	0.85	
					15	0.72	0.17	0.77	2.1	
	Mice	male	60 µg/g	Harderian	1	0.14	0.0023	0.20	1.3	
	(C3AF1)				15	0.13	0.0016	0.18	1.8	
		female	60 µg/g	Harderian	1	0.43	0.019	0.52	2.5	
					15	0.81	0.15	0.85	3.4	
		male	120 µg/g	Harderian	1	0.065	0.0010	0.086	1.0	
					15	0.29	0.0050	0.40	2.8	
		female	120 μg/g	Harderian	1	0.074	0.0012	0.094	1.2	
					15	0.064	0.0012	0.081	0.90	
	Mice	male	60 μg/g	Stomach	1	0.28	0.0091	0.34	2.4	
	(B6C3F1)				15	1.9	0.61	1.82	8.7	
		female	60 µg/g	Stomach	1	0.21	0.0083	0.26	1.1	
					15	0.19	0.0072	0.24	1.0	
		male	120 µg/g	Stomach	1	0.16	0.0059	0.20	0.90	
					15	1.2	0.50	1.2	2.9	
		female	120 µg/g	Stomach	1	0.58	0.19	0.60	1.5	
					15	1.6	0.67	1.6	3.7	

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						Ratio of	Juvenile	to Adult P	otency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
ENU (cont.)	Mice	male	60 µg/g	Stomach	1	0.046	0.0009	0.063	0.51	•
	(C3AF1)				15	0.35	0.023	0.41	1.3	
		female	60 µg/g	Stomach	1	0.81	0.085	0.89	3.5	
					15	1.1	0.19	1.1	4.5	
		male	120 μg/g	Stomach	1	0.16	0.010	0.19	0.56	
					15	0.69	0.32	0.70	1.5	
		female	120 μg/g	Stomach	1	0.44	0.14	0.46	1.2	
					15	0.63	0.24	0.64	1.5	
NMU	Mice	male	50 μg/g	lung adenomas	1	3.4	1.3	3.3	9.3	Terracini and Testa, 1970
	(BC3F1)	female	50 μg/g	lung adenomas	1	6.3	2.4	6.0	23	
		male	50 μg/g	lymphsarcoma	1	2.5	1.1	2.4	6.4	
		female	50 μg/g	lymphsarcoma	1	1.1	0.49	1.1	2.4	
		male	50 μg/g	hepatoma	1	35	6.5	32	324	
		female	50 μg/g	hepatoma	1	0.31	0.0023	0.39	13	
		male	50 μg/g	Renal adenoma	1	0.86	0.0093	1.2	13	
		female	50 μg/g	Renal adenoma	1	1.3	0.0081	1.7	33	
		male	50 μg/g	forestomach	1	0.032	0.0006	0.039	0.52	
		female	50 μg/g	forestomach	1	0.11	0.0027	0.15	0.69	

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	Ratio of Juvenile to Species, See Base Turner Base Geometric 3 50/								otency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	1
NMU (cont.)	Mice	male	25 µg/g	thymic lymphoma	1	1.9	0.048	2.1	23	
	(C3Hf/Dp)	female	25 μg/g	thymic lymphoma	1	1.2	0.0089	1.5	30	
		male	25 µg/g	lung adenomas	1	0.95	0.013	1.2	11	
		female	25 μg/g	lung adenomas	1	0.38	0.018	0.46	1. 7	
		male	25 μg/g	liver tumor	1	0.16	0.0016	0.21	4.6	
		female	25 μg/g	liver tumor	1	0.26	0.0026	0.39	4.4	
		male	25 μg/g	Stomach	1	0.47	0.0045	0.67	6.8	
		female	25 μg/g	Stomach	1	0.32	0.0046	0.43	3.8	
				ovarian	1	0.13	0.0014	0.17	3.5	
				uterine/vaginal	1	8.6	1.1	8.1	97	
		male	50 μg/g	thymic lymphoma	1	7.9	3.1	7.4	30	
		female	50 μg/g	thymic lymphoma	1	3.1	1.3	3.0	7.8	
		male	50 μg/g	lung adenomas	1	0.042	0.0008	0.058	0.45	
		female	50 μg/g	lung adenomas	1	0.059	0.0012	0.084	0.53	
		male	50 μg/g	liver tumor	1	0.25	0.0021	0.33	7.8	
		female	50 μg/g	liver tumor	1	0.11	0.0011	0.13	4.5	
		male	50 μg/g	Stomach	1	0.011	0.0003	0.013	0.12	
		female	50 μg/g	Stomach	1	0.11	0.0022	0.15	0.96	
				ovarian	1	0.011	0.0003	0.014	0.14	
				uterine/vaginal	1	0.028	0.0005	0.034	0.46	
		male	50 μg/g	thymic lymphoma	21	4.3	1. 6	4.1	17	
		female	50 μg/g	thymic lymphoma	21	1.0	0.39	1.0	2.6	
		male	50 μg/g	lung adenomas	21	0.14	0.0022	0.22	1.1	
		female	50 μg/g	lung adenomas	21	0.74	0.30	0.75	1.7	
		male	50 μg/g	liver tumor	21	0.12	0.0013	0.15	4.3	
		female	50 μg/g	liver tumor	21	0.92	0.0051	1.4	23	
		male	50 μg/g	Stomach	21	0.057	0.001	0.08	0.64	
		female	50 μg/g	Stomach	21	1.8	0.77	1.8	4.7	
				ovarian	21	0.044	0.0007	0.055	0.97	
				uterine/vaginal	21	1.7	0.59	1.7	6.4	

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						Ratio of	Juvenile	to Adult P	otency	
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.
Urethane	Mice	male	1 mg/g	liver	1	24	4.4	21	220	Chieco-Bianchi et al.,
	(Swiss)	female	1 mg/g	liver	1	0.44	0.0044	0.54	13	1963
		male	1 mg/g	liver	5	14	2.4	13	137	
		female	1 mg/g	liver	5	1.2	0.017	1.4	26	
		male	1 mg/g	liver	20	0.23	0.0018	0.28	10	
		female	1 mg/g	liver	20	0.10	0.0011	0.12	4.8	
		both	1 mg/g	skin	1	0.24	0.0027	0.32	5.4	
Urethane + croton oil	Mice (Swiss)	both	1 mg/g	skin	1	2.9	1.2	2.8	8.2	·····
Urethane	Rats (MRC	male/ female	16%x6	neurilemmomas	1	0.24	0.0028	0.33	4.5	Choudari Kommineni et al., 1970
	Wistar- derived)	male/ female	16%x6	neurilemmomas	28	0.39	0.0045	0.51	6.3	
		male/ female	16%x6	liver	1	7.9	1.4	7.1	82	
		male/ female	16%x6	liver	28	0.23	0.0026	0.4	11.7	
		male/ female	16%x6	thyroid	1	0.032	0.0006	0.039	0.67	
		male/ female	16%x6	thyroid	28	0.079	0.0011	0.1	1.5	
	Mice (Swiss)	male/ female	1 mg/g	lung	1	15	1.2	11	997	De Benedictis et al., 196
	Mice		***************************************	leukemia		6.7	1.7	6.1	45	Fiore-Donati et al., 1962
	(Swiss)					5.1	1.1	4.7	38	
										Continued next page

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						Ratio of Juvenile to Adult Potency					
Compound	Species, strain	Sex	Dose	Tumor	Day	Geometric Mean	2.5%	Median	97.5%	Refs.	
Urethane (cont.)	Mice (B6AF1/J)	male	1 mg/g	liver	21	5.1	1.4	4.7	30	Klein, 1966	
		female	1 mg/g	liver	21	0.20	0.0019	0.26	6.0		
				Harderian gland	1	0.26	0.0021	0.33	11		
					7	0.26	0.0021	0.33	11		
					14	0.64	0.0044	0.85	20		
		male	1 mg/g	Harderian gland	21	0.32	0.0024	0.41	13		
		male	1 mg/g	Forestomach	1	0.065	0.0009	0.079	1.9		
		female	1 mg/g	Forestomach	1	0.36	0.0028	0.49	11		
		male	1 mg/g	Forestomach	7	0.15	0.0017	0.19	3.5		
		female	1 mg/g	Forestomach	7	0.13	0.0013	0.16	5.0		
		male	1 mg/g	Forestomach	14	0.16	0.0018	0.21	3.9		
		female	1 mg/g	Forestomach	14	0.79	0.0056	1.1	18		
		male	1 mg/g	Forestomach	21	0.060	0.0008	0.072	1.7		
	Mice (B6AF1/J)	female	1 mg/g	Forestomach	21	0.16	0.0015	0.2	6.3		
				lung	1	0.95	0.36	0.95	2.5		
		male	1 mg/g	lung	14	0.79	0.26	8.0	2.3		
		female 1 mg	1 mg/g	g lung	14	0.44	0.16	0.45	1.1		
					21	0.86	0.31	0.86	2.4		
	Mice (C3H/f)	male	1 mg/g	liver	1	14	4.0	12	81	Liebelt et al., 1964	
		female	1 mg/g	liver	1	16	3.2	15	155		
		male	1 mg/g	lung	1	5.9	1.7	5.6	28		
		female	1 mg/g	lung	1	22	4.5	20	203		
		male	1 mg/g	reticular tissue	1	2.0	0.023	2.3	38		
		female	1 mg/g	reticular tissue	1	8.6	2.3	7.7	60		
	Mice (Swiss)		1 mg/g	pulmonary adenomas	2vs4 weeks	14	1.1	10.1	965	Rogers, 1951	
			1 mg/g	pulmonary adenomas	2vs6 weeks	16	1.3	11.3	1025		
			1 mg/g	pulmonary adenomas	2vs8 weeks	19	1.6	13.3	1126		
			1 mg/g	pulmonary adenomas	2vs10 weeks		1.9	14.5	1168		
			0.25 mg/g	adenomas	3vs8week	7.1	2.3	6.7	29		
			0.5 mg/g	adenomas	3vs8week	0.67	0.29	0.67	1.6		
			1.0 mg/g	adenomas	3vs8week	0.68	0.28	0.68	1.6		